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SURGERY

A Monthly Journal Devoted to the Art and Science of Surgery

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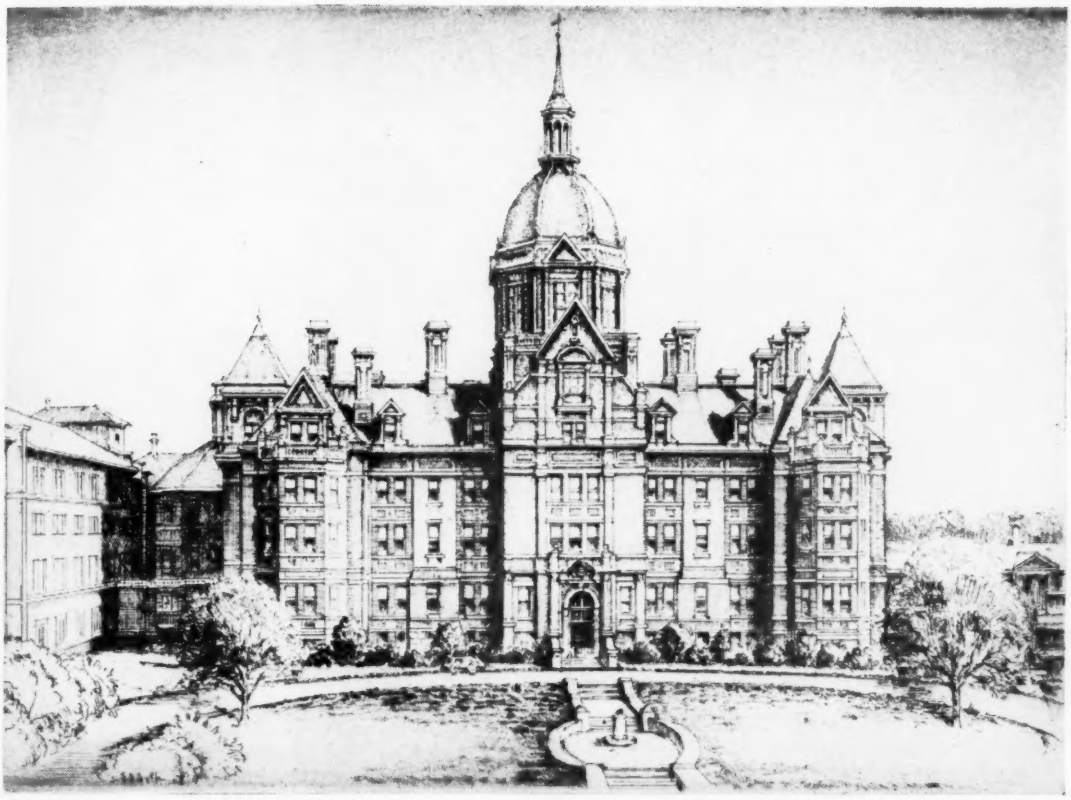

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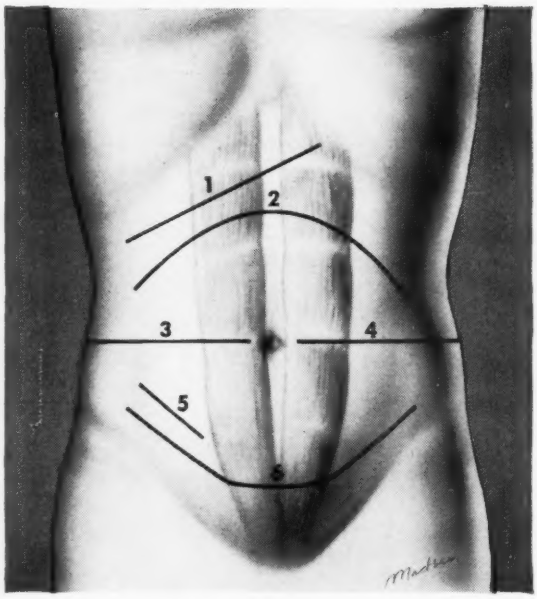

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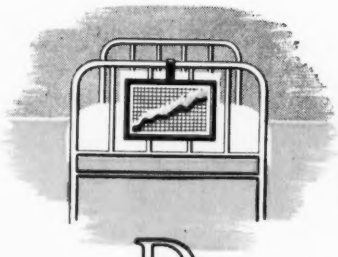

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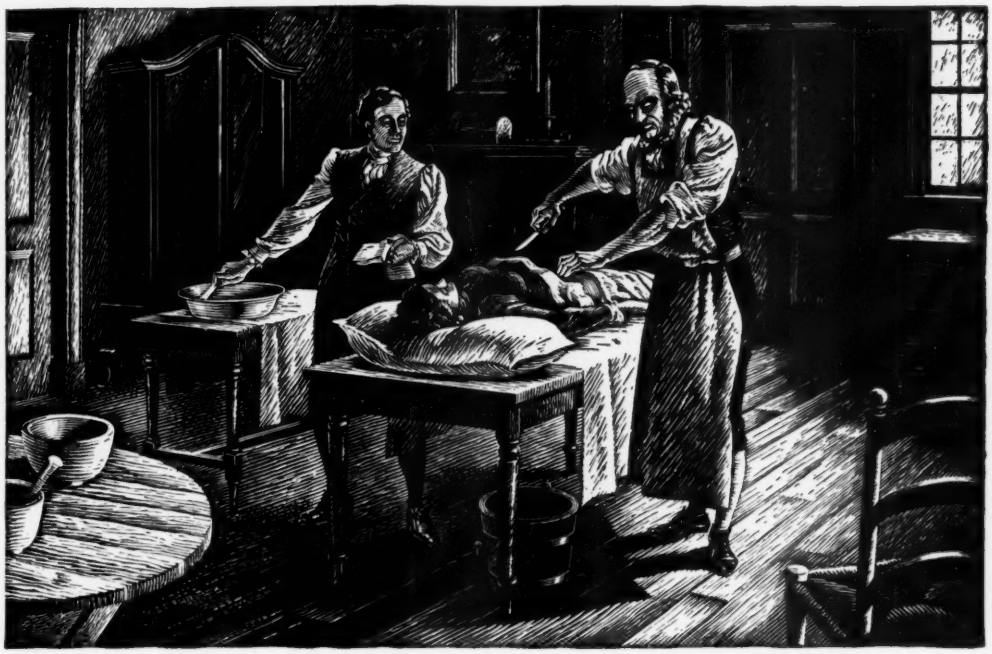

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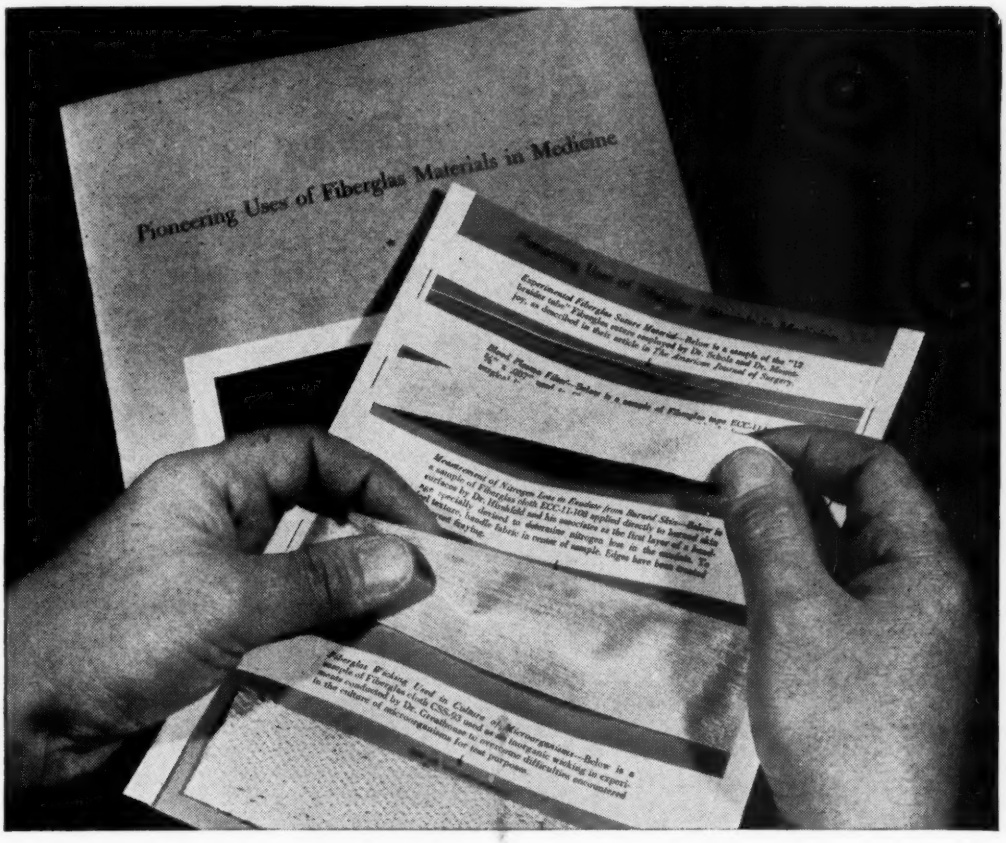

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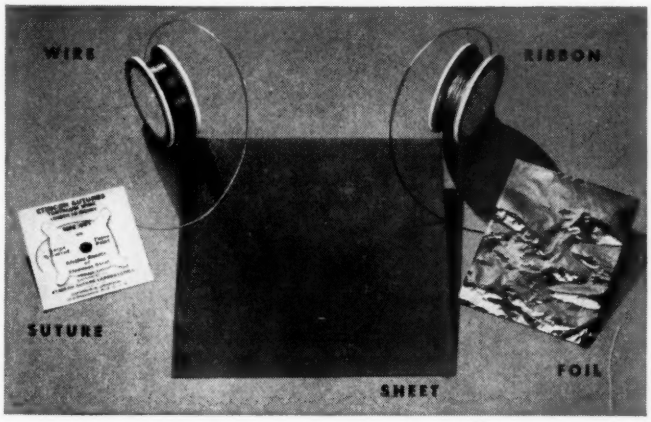

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SURGERY

VOL. 17 JANUARY, 1945 NO. 1

Original Communications

TRAUMATIC PERFORATION OF THE COLON AS SEEN IN A GENERAL HOSPITAL

MAJOR BENTLEY P. COLCOCK, MEDICAL CORPS, U. S. ARMY

THE mortality rate following traumatic perforation of the colon in World War II has dropped to the neighborhood of 33 per cent. This represents a marked improvement over the mortality figures for World War I, which, in this type of patient, ranged from 50 to 75 per cent, and is largely due to the early replacement of blood loss by plasma, and particularly whole blood, the intraperitoneal use of the sulfonamides, and the excellent surgery being done by the well-trained abdominal surgeons in our forward field and evacuation hospitals.

That an uncomfortably high morbidity still exists in this group of cases is not generally appreciated except by those surgeons working in the general and other hospitals back of the forward areas. Few of the patients treated here recover without some type of complication such as wound infection, wound separation, retraction of the colostomy, evisceration, or the development of abdominal wall, intra-abdominal, subphrenic, and retroperitoneal abscesses. Most of them have a prolonged convalescence extending over a period of two or three months. After this period of convalescence, many have to be evacuated to the zone of the interior for major intra-abdominal surgical procedures to restore intestinal continuity. These additional procedures are associated with an accepted mortality rate of from 8 to 10 per cent. The ingenuity of the surgical staff is frequently taxed to the utmost in order to prevent certain complications from progressing to a fatal termination. It is my considered opinion that with further experience and particular attention to certain details in the primary treatment of these patients, the reduction in the mortality rate can be followed by a corresponding reduction in the morbidity rate.

The following suggestions are made on the basis of a rather extensive experience with the Mikulicz procedure in the treatment of carcinoma of the colon in civilian life, modified by the experience gained from the

Received for publication, June 9, 1944.

study and care of a group of twenty-three patients with traumatic perforation of the colon who had been evacuated to North Africa from the Italian theatre of operations.

The fundamental principles concerning the treatment of battle casualties with perforation of the colon must first be stated: (a) It is generally accepted today that the safest method of dealing with a laceration of the colon is by exteriorization of the lacerated segment of bowel. (b) The primary object in the treatment of these patients in the forward area is the saving of life, and the setting up of conditions which will facilitate the further care of that patient is secondary. The facts and the problems confronting the surgeon in the forward area have been kept in mind at all times in the following discussion, although, as already pointed out, the secondary complications occurring in these patients may be sufficiently grave so as to actually jeopardize the life of the patient.

The most important step in the exteriorization of the colon is the adequate mobilization of the bowel. In the first place, this greatly facilitates the exteriorization of the entire injured segment. It must be kept in mind that frequently a considerable area of bowel wall surrounding the actual perforation has been devitalized by the trauma, and will subsequently slough. It is equally important that the entire injured area must be exteriorized without tension. If tension on the bowel is necessary to bring the segment above the skin level, it will inevitably retract. If this retraction stops at the skin level nothing more serious than a constricted colostomy stoma may result. This often functions poorly, and renders the subsequent examination and clamping of the spur much more uncomfortable for the patient. If the retraction proceeds below the skin level, it leads to infection of the wound with partial or complete separation. This, in turn, may lead to evisceration. If the retraction extends below the peritoneal level as in one of our patients, local or generalized peritonitis results with the frequent formation of intraperitoneal, pelvic, or subphrenic abscesses. In seven of our patients the colostomy stoma was at the level of the skin or beneath. Five of these men had abscesses in the abdominal wall with partial or complete separation of the abdominal incision. Two developed subphrenic abscesses (bilateral in one case), and one patient eviscerated. The operative notes occasionally mentioned the fact that tension was necessary to exteriorize the bowel.

The following brief résumé of the clinical course of one of these patients illustrates how a series of complications occurred, each of which almost cost the patient his life. A few more minutes spent on mobilization of the colon might have prevented these complications.

A soldier was wounded in the left flank, Nov. 3, 1943, by enemy shell fragments. Fortunately, due to the proximity of a field hospital, he was operated upon within three hours after his injury. Through a left posterolumbar incision, thirteen perforations of the ileum and jejunum were closed and four inches of the

descending colon removed because of two perforations at that point. There was not sufficient mobility present for exteriorization through an anterior stab incision, so the two loops of colon were brought out through the operative incision in the left flank. He was admitted to the general hospital, Nov. 13, 1943, with a temperature of 101° F., vomiting occasionally, but taking some liquids by mouth. His wound was completely separated, with the sutures lying loose in it. The colostomy loops had separated and retracted below the peritoneal level, exposing the dorsal musculature, the layers of the abdominal wall, and the adjacent peritoneal cavity to constant fecal contamination. The adjacent loops of small bowel were covered by granulation tissues. Fever continued and Nov. 29, 1943, a right subphrenic abscess was discovered and drained. (The predominant organisms were *Bacillus coli* and *Bacillus clostridia*.) He improved temporarily, but again became febrile, and his condition deteriorated. Sterile pleural effusion, 500 c.c., was aspirated from the right side of the chest, Dec. 3, 1943, and 900 c.c. of a similar amber-colored fluid was aspirated from each pleural cavity, Dec. 7, 1943. His temperature rose to 101 to 102° F. at night, pulse remained at 110 to 120, and his feet and back became edematous. Dec. 11, 1943, an abscess lying between the abdominal wall and the peritoneum, and extending medialward from the incision across the midline, was incised and drained (predominant organism again *B. coli*). He again became febrile after a short period of improvement. Dec. 16, 1943, 1,000 c.c. of clear amber-colored fluid were aspirated from the left pleural cavity and 750 c.c. from the right side. Dec. 22, 1943, a retrocecal abscess was drained of 200 c.c. of thick white pus. In spite of this, there was no essential change in his condition which continued critical. X-ray examination, Dec. 26, 1943, showed a small bubble beneath the left diaphragm, and a left subphrenic abscess was drained, but the patient again failed to make any permanent or sustained improvement. Jan. 6, 1944, pus was obtained from the left pleural cavity. It was loculated posteriorly and was drained by a thoracotomy. He now began to show the first definite and sustained improvement, but continued to have a low-grade fever. He was given 300,000 units of penicillin. (The sulfonamides had been discontinued long before because of their tendency to accelerate the fall in the red blood cell level, which was being sustained by repeated blood transfusions.) Possibly due to the penicillin, but probably to the fact that we had finally drained the last abscess, he continued to improve, his temperature fell to normal, and he became ambulatory by the time he was evacuated to the zone of the interior. His wound had finally healed but he will require a major intra-abdominal procedure to restore intestinal continuity because of the widely separated and retracted colostomy loops.

Mobilization of the large bowel by division of its lateral peritoneal attachments is a relatively avascular procedure. The only blood vessels which may need to be clamped and divided are a few at the splenic and hepatic flexures. After the line of fusion between the peritoneum covering the bowel and the lateral parietal peritoneum has been incised (see Fig. 1), the bowel and its mesentery are easily mobilized medialward by sharp and blunt dissection. This provides ample bowel for exteriorization of the proximal and distal loops, even if resection of several inches or more of bowel should be necessary. The retroperitoneal second portion of the duodenum will be encountered on the right side, and should be carefully reflected posteriorly. The ureter on the side involved, should, of course, be found and preserved. An excellent guide to the ureters is the spermatic vessels cross-

ing anterior to the ureter directly below the kidney pelvis and lying just lateral to it throughout its course down to the pelvis. These vessels are easily identified as the dissection proceeds medialward, and the ureter will be found 1 cm. or less further toward the midline (see Fig. 2*B*). In exteriorization of the splenic flexure, the jejunum at the ligament of Treitz will often be exposed and injury to it should be avoided. The mesentery of the colon will become rather thin and delicate as it is reflected from the posterior abdominal wall and care must be taken lest it be perforated by the retracting fingers. Any perforations should, of course, be closed to prevent possible herniation of small bowel through the aperture. Little, if any, dissection is usually necessary in liberation of the sigmoid colon. With wounds of the ascending

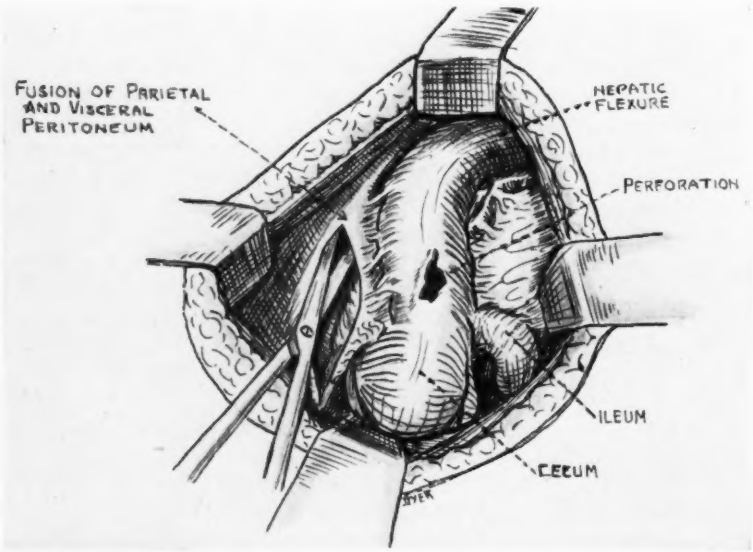

Fig. 1.—Showing the first step in mobilization of the right colon by incision of the peritoneum along the avascular line of fusion between the visceral and lateral parietal peritoneum.

colon, the hepatic flexure must be detached, and in the case of the descending colon, liberation of the splenic flexure in addition to the division of the lateral attachments will provide adequate mobilization (see Fig. 3). The amount of dissection necessary with wounds of the transverse colon depends largely on its redundancy. The omentum has an avascular attachment to the transverse colon and can be easily removed. Even the necessary liberation of both flexures should not prolong the operative procedure unduly in most cases and with the adequate exposure that is essential in these patients, it should add but five to ten minutes to the operating time. Because of the possibly increased risk of wound infection from the ileostomy, there is a question in the minds of some authorities as to whether it is safe to exteriorize the right colon and construct a double-barreled ileocolostomy by approximation of the terminal ileum to the ascending or transverse colon. This certainly can be done without increased risk of wound

infection when operating for carcinoma of the cecum and ascending colon in civilian practice. Two patients of this group had had a procedure of this type. One had no infection of his wound. The ileocolostomy had been clamped and closed, and he was returned to duty. A second patient had a moderate infection of his wound with separation of the skin and subcutaneous layers. The ileocolostomy had been

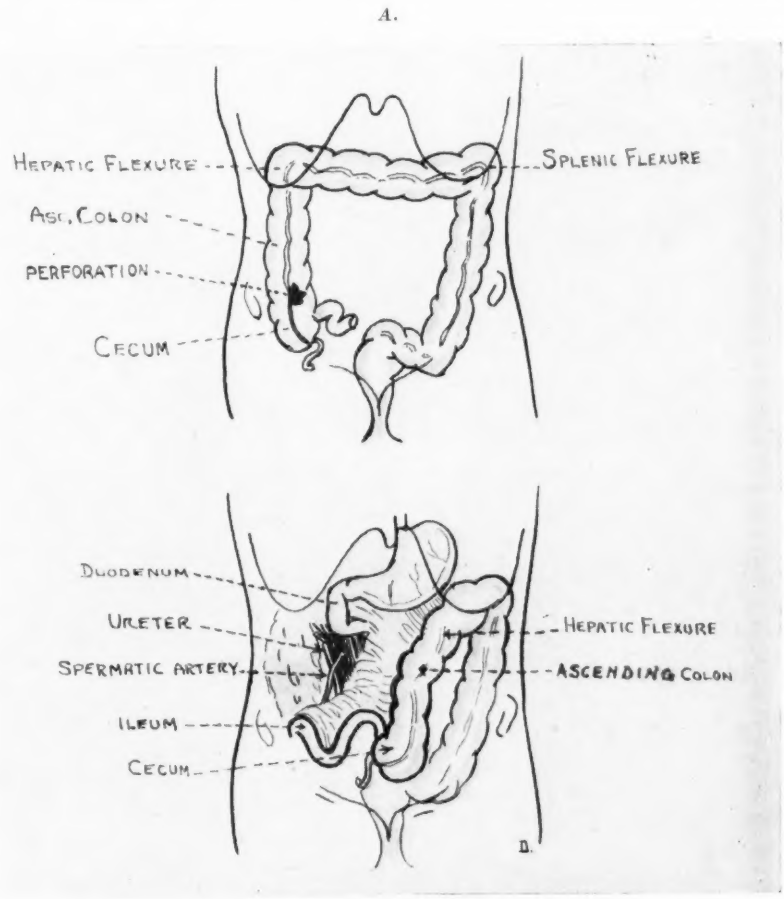

Fig. 2.—*A*, Schematic representation of a perforating wound of the ascending colon. *B*, Mobilization of the right colon, showing the retroperitoneal portion of the duodenum, right ureter, and right spermatic vessels, as the mesentery is reflected from their anterior surfaces.

clamped and closed without difficulty, and the abdominal wall is now in good condition. A third patient with extensive wound of the ascending colon had a right lower quadrant ileostomy and an epigastric transverse colon colostomy. The wounds healed perfectly, but he had to be evacuated to the zone of the interior with the added nursing care that an ileostomy requires. He still faces a major intra-abdominal procedure with an associated mortality between 5 and 10 per cent. Complete information on all of these cases involving the right colon cases will be required to settle definitely this point.

In the second place, adequate mobilization of the bowel permits the rapid formation of a five- or six-inch double-barreled colostomy spur (see Fig. 4). This, in turn, makes it possible to restore intestinal continuity at a later date, by a minor extraperitoneal procedure. Two rows of sutures uniting the two loops facilitate the subsequent clamping of the partition. If haste is imperative, one row of sutures is sufficient to prevent the small bowel or omentum from inserting itself between the loops of the spur, and the partition can be clamped without

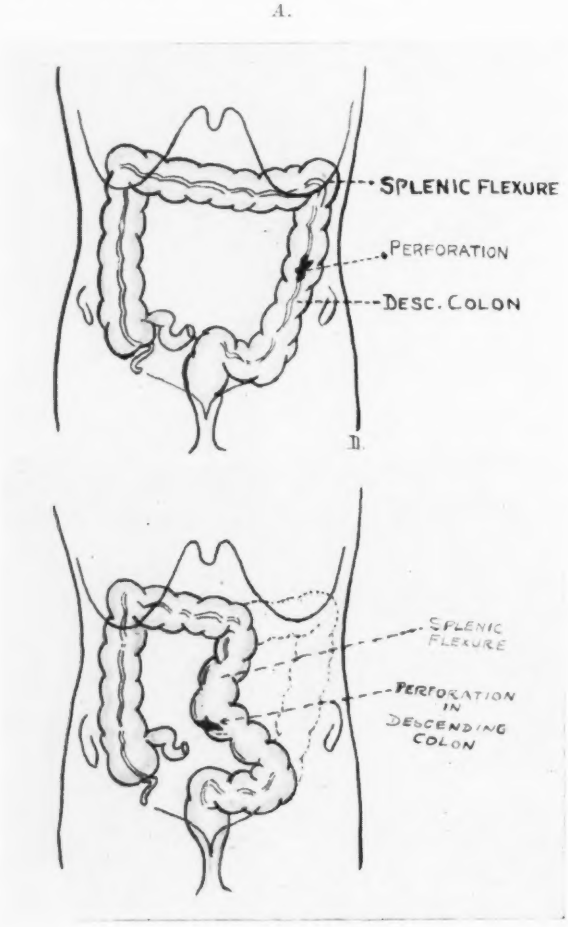

Fig. 3.—*A*, Schematic representation of a perforating wound of the descending colon. *B*, Showing mobilization of the left colon by freeing the descending colon, splenic flexure, and the distal portion of the transverse colon.

risk (see Fig. 5). These sutures should not be passed into the lumen of the bowel. There is no tension of this suture line and approximation is all that is required. Uniting the longitudinal bands of the colon by seromuscular sutures tied without constriction of the tissue permits the formation of a double-barreled colostomy which involves no added risk from peritonitis, and which is ideal from the point of view of the

later restoration of intestinal continuity. A five- or six-inch spur not only permits the colostomy stoma to be brought well (one and one-half to two inches) above the skin level, but also insures an adequate bowel lumen after the subsequent closure (see Fig. 6). There will be no postoperative leakage of intestinal content if the spur is made of sufficient length in the first place and the bowel wall is rendered sufficiently

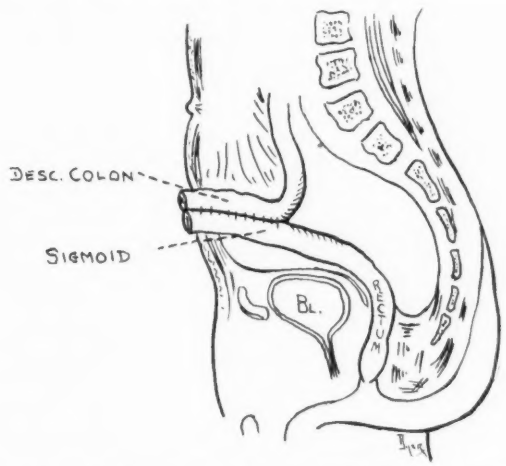

Fig. 4.—Schematic Sagittal view of the construction of a double-barreled colostomy spur for a perforation low in the sigmoid colon. This may necessitate mobilization of the upper rectum and rectosigmoid portion of the colon.

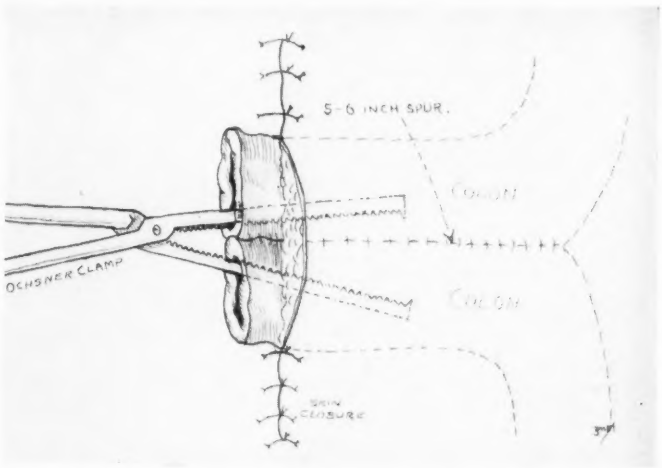

Fig. 5.—Schematic representation of the colostomy spur, and the application of the straight Ochsner clamp. It will usually require two or three applications of the clamp for complete division of the spur.

pliable by removal of all scar tissue at the time of closure, so that it can be inverted without tension. It was possible, by slow and careful clamping of the partition, to secure sufficient lumen to permit extraperitoneal closure in approximately 50 per cent of our patients, although only a few had approximation (by sutures) of the two loops at the time of the original operation. Three other patients were evacu-

ated because of unhealed osteomyelitis of the sacrum, and one because the two loops were crossed, making it impossible to clamp the partition without destroying the blood supply to the bowel. No complications occurred which could be attributed to the clamping or closure, and there has been no mortality among our patients with perforated colons. One patient had leakage of intestinal content postoperatively, which was probably due to the combination of a short spur, plus the formation of an abscess postoperatively in the old sinus tract made by the shrapnel fragment, which communicated with the wound of closure.

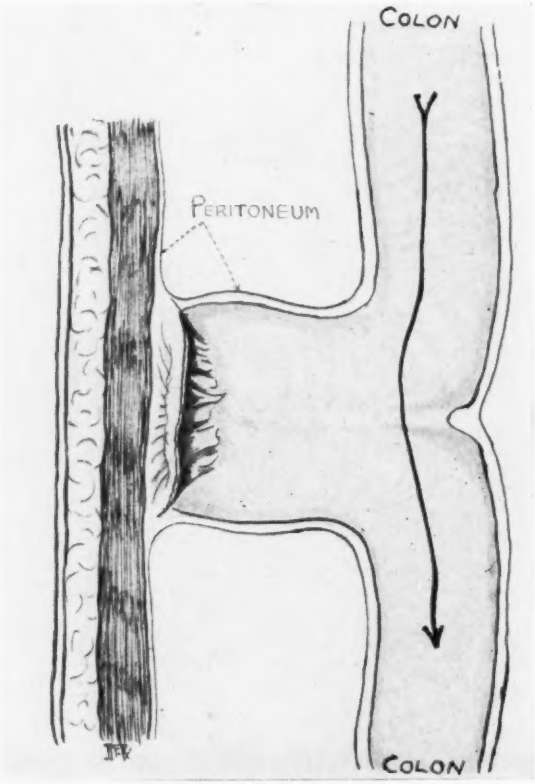

Fig. 6.—Schematic representation of the intestinal lumen following closure. The peritoneal cavity has not been opened, and the muscle, fascia, and skin layers of the abdominal wall have been approximated over the inverted colostomy stoma.

(Those patients whose colostomies have been closed have been returned to Class B duty in this theatre of operations. Several, who were technical sergeants, have been returned to work similar to that carried on before their injury.) More of the colostomies could have been closed and the patients returned to duty, and the subsequent care in the group that was salvaged would have been rendered infinitely safer and easier had it been possible to construct an adequate double-barreled spur at the time of the original operation.

The incidence of infection in these wounds is high, because we are dealing with an open wound in the colon, frequently associated with

gross soiling of the peritoneal cavity by fecal material. Because of this fact, some surgeons have felt that complete closure of the laparotomy incision with exteriorization of the bowel through a lateral stab wound decreases the incidence of infection and separation. In the original incisions in our small series, the incidence of infection was equal (5 per cent) in the group with the stab wound colostomy and in the group with the colostomy in the laparotomy incision. Whether the additional time and manipulation required in the former group are justified remains to be settled when the collected statistics from all hospitals are analyzed. This is also true of other impressions of ours, such as the advisability of the use of through-and-through sutures without closure of the wound in layers. It is certainly important that these patients should have a minimum of transportation, not only until they have passed the critical stage, but until they have good wound healing. Certainly it is true that any and all measures designed to decrease contamination and to achieve primary healing of the incision are to be commended because infection with the frequently associated separation of the wound markedly prolongs the convalescence of these patients.

The following is an illustrative case.

A 28-year-old artilleryman sustained a penetrating wound of the left side of his abdomen, Nov. 11, 1943. At operation, four hours later, a wound of the jejunum was found and closed, a wound of the splenic flexure of the colon was exteriorized, and a retroperitoneal hematoma drained. In order to provide more adequate exposure, a transverse incision was added to the left rectus incision. A wound infection developed and on the fourteenth day, after coughing, he eviscerated. Following closure, he began to show evidence of a more serious infection, with necrosis of the adjacent tissues of the abdominal wall. A microaerophilic streptococcus was found which responded to zinc peroxide, but much of the abdominal wall was lost and the colostomy retracted below the skin level.

Dec. 20, 1943, he was admitted to a general hospital in fair condition, with a large granulating wound, nine by six inches, oval in shape. The colostomy, just to the left of the wound, was below the skin level, but was functioning well. There was a purulent discharge from a sinus tract just lateral to the colostomy. Temperature was 101° F. Dec. 29, 1943, a retroperitoneal abscess was drained through the left flank. The patient improved temporarily, but again became febrile, with a deterioration in general condition. Jan. 2, 1944, a posterior right subphrenic abscess was drained through the bed of the twelfth rib. He immediately began to improve and his temperature dropped to 100° F. Jan. 5, 1944, he disrupted the large granulating abdominal wound, and eviscerated for the second time. The stomach, several feet of small bowel, and the tranverse colon were replaced in the abdominal cavity and the wound closed under considerable tension. After a critical period of two or three days he gradually rallied, but the wound partially separated, and on Jan. 12, 1944, he developed a high jejunal fistula in the center of the granulating area. In spite of various temporary measures designed to by-pass the jejunostomy, the opening in the bowel became larger and his condition again became critical. March 10, 1944, the fistulous area in the jejunum was resected and end-to-end anastomosis performed; a fourth attempt to close the abdominal wall was carried out. The colostomy, which was situated at the margin of the wound, was moved further into the flank to facilitate closure

and to decrease the subsequent contamination of the incision. The closure was partially successful due to necrosis and slough of the wound margins in the central portion, but the fistula has remained closed, and the patient is making satisfactory recovery at the time of this report.

The tremendous amount of supportive treatment necessary to carry these patients over each of their complications has not been mentioned, but can readily be imagined. The technical treatment of many of their complications is usually not difficult, but the diagnosis is often exceedingly difficult. These patients have all been through so much that their margin of safety is small and one must be constantly on the alert to detect even slight changes in their general condition. A slight elevation in a temperature curve which has been falling may indicate a new abscess which must be found and drained quickly, for it may be just "the straw which breaks the camel's back."

Thanks to the technical skill of the surgeons operating in the forward areas, it is now possible to state that the majority of patients sustaining a perforating wound of the colon will survive. We feel that before long it will also be possible to state that the majority of these patients will not have to be evacuated to the United States, but can be restored to useful duty in the theatre of operations, with no increase in the over-all mortality rate.

CONGENITAL ABSENCE OF THE GALL BLADDER

CLAUDE F. DIXON, M.S., M.D.,* AND A. L. LICHTMAN, M.D.†
ROCHESTER, MINN.

INTERESTING findings in a case of congenital absence of the gall bladder observed recently at the Mayo Clinic prompted a study of all of the cases of this anomaly that have been observed at the clinic and a review of the cases that have been reported in the literature. The cystic duct also was absent in most of the cases which form the basis of this report. This was the only concomitant anomaly of the extrahepatic bile ducts that was present in any of the cases. Anomalies of the extrahepatic bile ducts constitute another problem. They usually are found in stillborn infants or in infants born with icterus. They frequently are associated with other anomalies.

Many of the reports of congenital absence of the gall bladder were found to be inadequate for study. Many older reports consist only of statements that were made before some society.[1, 2] In some articles that otherwise were satisfactory, there was no mention of the status of the extrahepatic bile ducts and in some cases in which the anomaly was found at operation there was no means of ruling out the presence of an intrahepatic gall bladder. In an occasional report, the author mentioned having seen several other cases but did not describe the findings.

In 1902, Gay[3] reviewed nineteen cases of congenital absence of the gall bladder that had been reported in the literature. Buddy[4] and Theodor[5] surveyed the German literature and the latter author reported a case which he had observed personally. Bower,[6] in 1928, collected thirty-five cases from the literature and in four of these cases the cystic duct was present. He also reported a case which he had observed. Gross,[7] in reporting a case of double gall bladder, in 1936, reviewed the literature on congenital anomalies of the gall bladder and summarized the findings in thirty-eight cases that had been reported since 1905. One may add the cases of Danzis,[8] Fowler,[9] Theodor,[5] Torrance,[10] and Whipple[11] to those mentioned by Gross.[7] In addition, Whipple mentioned two other cases which he had observed previously. Since 1936, thirteen additional cases have been reported[12-17] but reports of two of these cases were not available to us.[18-20] Thus, we were able to obtain thirty satisfactory reports that were made before 1900 and fifty that have been made since that time. To these cases that have been reported in the literature, we wish to add ten cases that have been observed at the Mayo Clinic.

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The embryology of the gall bladder has been described adequately by Keibel and Mall.[21] Two theories have been advanced to explain congenital absence of the gall bladder.[7] The first of these is that the anomaly is due to failure of the gall bladder bud to develop from the hepatic diverticulum. This failure also would result in an absence of the cystic duct. The second theory maintains that the anomaly is due to failure of the gall bladder bud to resolve from its solid embryonic stage. The presence of a solid cord residue would favor the latter theory.

From comparative anatomy one learns that in the Petromyzon, the pigeon, and the rat the gall bladder diverticulum is present but disappears as the embryo matures. There are conflicting reports on the presence of the gall bladder in some species of animals. It probably is reasonable to assume that the gall bladder usually is absent in these species, which include the giraffe, the camel(?), and the elephant(?).[2, 16] According to Mentzer,[22, 23] the gall bladder has been said to be absent uniformly in twenty-six species of mammals including the goat, deer, rat, rhinoceros, peccary, pilot whale, hyrax,[24] two-toed and three-toed sloth, and the horse, ass, and mule, seventeen species of fish including the Petromyzon or the lamprey, which is a cyclostome, and nine species of birds including the dove and pigeon. It is interesting to note that, with the exception of the pilot whale, the mammals which normally do not have a gall bladder are predominantly vegetarian and depend on ingested carbohydrate for their body fat.

Many of the reports of cases of congenital absence of the gall bladder that appeared before 1900 were rather cursory and the cases differ from those reported since 1900. Such data as are available will be presented briefly. In twenty-four of the thirty cases the anomaly was found at necropsy; in two of the cases it was found at operation and confirmed at necropsy, which followed closely; while in four cases it was not stated whether the anomaly was found at necropsy or at operation. In five of the twelve cases in which an adequate history was obtainable, symptoms suggestive of cholecystic disease were present. Jaundice was present in six cases. The common duct was found to be dilated in five of the ten cases in which the size of the duct was mentioned. The cystic duct was present in four cases and noted as absent in thirteen cases. Stones were found in two cases. Twelve of the patients were females and ten were males. Eight infants were included, while in ten cases the patients were more than 45 years of age. Many of the cases in which the patients were infants were eliminated because of extensive associated anomalies.[25]

The reports that have appeared since 1900 are more complete than those which were made previously. The anomaly definitely was stated to have been found at operation in two of the thirty cases reported

prior to 1900, but it was discovered in this manner in thirty-four of the sixty cases* reported subsequently. An element of doubt is introduced when the anomaly is observed at operation, but in six of the cases in which the anomaly was observed in this manner it subsequently was confirmed at necropsy. In this study we did not include cases in which a small pouch was seen on the common duct. In a few cases (for example, in the one reported by Miller),[26] there was a nubbin of the common bile duct which contained a stone. These cases were eliminated from consideration because of the likelihood that the nubbin represented the end result of inflammatory obliteration.

ANALYSIS OF CASES REPORTED SINCE 1900

Of the cases of this anomaly that have been reported since 1900, fifty were found satisfactory for study. To these fifty cases we wish to add ten cases which have been observed at the clinic. These cases will be reported briefly in this paper.

In twenty-six of the sixty cases the anomaly was found at necropsy and in the thirty-four remaining cases it was found at operation. In six of the thirty-four cases the presence of the anomaly subsequently was confirmed at necropsy. In the twenty-six cases in which the anomaly was found at necropsy, the following causes of death were mentioned: tuberculosis in five cases, lobar pneumonia or bronchopneumonia in five cases, and myocarditis in two cases. Syphilis was present in one case. As previously stated, in twenty-four of the thirty cases that were reported prior to 1900 the anomaly was found at necropsy. In five of these cases death was attributable to tuberculosis and in four cases it was due to pneumonia. It is evident that tuberculosis and pneumonia caused death in about the same percentage of cases in each group.

In twenty-four of the sixty cases the anomaly was found in the course of operation for suspected cholecystic disease. On four occasions it was disclosed by an exploratory laparotomy; in two cases a diagnosis of appendicitis was considered, and in four cases the anomaly was an incidental finding in operations on the stomach and duodenum.

The average age of the patients was 46.7 years. Forty-two of the patients were more than 45 years of age and four were less than 1 year of age. Thirty-six of the patients were females and twenty-three were males. In one case the sex of the patient was not mentioned.

Symptoms suggestive of cholecystic disease were present in thirty-five cases (in eight patients pain extended to the left side of the thorax and to the scapula). In thirteen cases the symptoms were not referable to the gall bladder and in twelve cases the symptoms were not described adequately. Jaundice was present in twenty-nine cases.

*This figure includes ten cases which have been observed at the Mayo Clinic.

In fifteen cases cholecystography failed to produce visualization of the gall bladder. Stones were seen in the region of the common bile duct in four cases.

The gall bladder fossa in the liver was present in seven cases and absent in twenty-five. It was not mentioned in twenty-eight cases. The cystic duct was present in four cases and absent in forty-two cases. It was not mentioned in fourteen cases. The common bile duct was dilated in nineteen cases and of normal size in twenty cases. In twenty-one cases mention of the size was omitted. In one of the cases there was a carcinoma of the common bile duct[15] with dilatation of the duct above the lesion.* Gallstones were found in the common bile duct or in the hepatic ducts in sixteen cases. Their absence was mentioned in nineteen cases, but not mentioned in twenty-five cases.

The liver was noted as enlarged in nine cases and as cirrhotic in thirteen cases. Hepatitis was noted in five cases and the left lobe was absent in one patient. An unusually small quadrate lobe was seen in six cases. The pancreas was mentioned in twelve cases. Pancreatitis was present in eleven cases. The pancreas was poorly developed in one patient and diabetes was present in four cases. No mention was made of changes in the spleen.

The sixty cases may be divided roughly into three groups. One group consists of cases in which the patients were infants. In this group the absence of the gall bladder was noted at necropsy. Jaundice was a common finding and the causes of death were described as "emaciation," bronchopneumonia, peritonitis, encephalitis, and an imperforate anus. In the second group of cases the patients were between infancy and 45 years of age and the anomaly usually was found at necropsy. Death frequently resulted from pulmonary disease. In 73 per cent of the cases in which the patients were past the age of 45 years, symptoms similar to those found in cholecystic disease were present. In the majority of the cases in the last group the anomaly was discovered at operation.

REPORTS OF CASES OBSERVED AT THE CLINIC

CASE 1.—A Norwegian woman, aged 61 years, had had attacks of jaundice, chills, fever, and pain in the left upper quadrant of the abdomen which had extended to the left scapula. Abdominal distress and belching had occurred after meals. These symptoms had been present for eight years. Cholecystography revealed nonfunctioning gall bladder. The value for the serum bilirubin was 6.5 mg. per 100 c.c. Analysis of the gastric contents disclosed an absence of free hydrochloric acid; the value for the total acidity was 6 according to the method of Töpfer. Cholecystic disease and biliary obstruction were suspected. Operation disclosed absence of the gall bladder and cystic duct. There was no gall bladder fossa in the liver. Three stones were found in the dilated common bile duct.

*Although the term "common bile duct" implies fusion of the cystic and hepatic ducts, it is used here to designate fusion of the hepatic ducts also. In two of the cases, two hepatic ducts proceeded independently into the duodenum. This may have been true in more cases but missed at operation.

A T tube was inserted into the common bile duct. The pancreas and liver were normal. The jaundice disappeared rapidly and the concentration of serum bilirubin decreased to 1.2 mg. per 100 c.c. in two weeks. The T tube was removed in two months. The patient was asymptomatic thereafter.

CASE 2.—A man, aged 68 years, of Norwegian descent, had had attacks of jaundice and of epigastric pain which extended to the sternum. These attacks had been present for six weeks and morphine had been required. Other symptoms included fever and chills, intolerance of fat, and a loss of sixty pounds (27.2 kg.). No jaundice was present at the time the patient was examined. The value for the serum bilirubin was 1.1 mg. per 100 c.c. Cholecystography did not reveal any gall bladder. Obstructive cholecystic disease was suspected. Operation revealed absence of the gall bladder. The common bile duct was of normal size and no stones were present. The liver was normal but pancreatitis, grade 3 (on the basis of 1 to 4, in which 1 designates the mildest and 4 the most severe condition), was present. A T tube was placed in the common bile duct. Recovery was excellent. After slow progressive clamping of the tube without symptoms being produced, the tube was removed two years after its insertion. A year later the patient was still asymptomatic.

CASE 3.—A woman, aged 29 years, of Norwegian descent, had colicky pain in the left side of the epigastrium, fever and chills for four years. Ingestion of food or vomiting had relieved the symptoms. She had lost twenty pounds (9.1 kg.). Roentgenologic examination of the stomach revealed a duodenal ulcer and a subacute perforating gastric ulcer. Operation disclosed hourglass stomach, two gastric ulcers, and a duodenal ulcer. Absence of the gall bladder was noted incidentally. The common bile duct was normal. A gastric resection was performed. Recovery was uneventful. Four years after resection the patient was well.

CASE 4.—A woman, aged 39 years, of Irish descent, had had attacks of gaseous distention, nausea, and vomiting which had been precipitated by ingestion of fatty foods. These attacks had been present for three years. There was pain in the right side at the level of the umbilicus. Jaundice was not present. Roentgenologic examination of the stomach did not disclose any abnormality. Disease of the gall bladder was suspected. Operation disclosed absence of the gall bladder and cystic duct. The common bile duct was moderately dilated but it was not explored. The position of the duct was normal. The appendix was removed and the pathologist reported the presence of catarrhal appendicitis. Two years later the patient stated that the symptoms still were present.

CASE 5.—A man, aged 53 years, had had pain in the upper part of the abdomen and bloating after meals for ten years. The pain had been most intense in the left subcostal region. Tenderness had been noted over the right upper quadrant of the abdomen. Some of the symptoms had been relieved by taking bicarbonate of soda. On many occasions, morphine had been required to relieve the pain. There had not been any jaundice or vomiting. Although roentgenologic examination of the stomach disclosed a duodenal ulcer, a diagnosis of cholecystic disease was considered. Operation disclosed absence of the gall bladder. The appendix had been removed previously. A duodenal ulcer was present. The gall bladder fossa in the liver was present and the common bile duct was of normal size. A posterior gastroenterostomy was performed. The patient returned four, and again seven years, after the operation. On each of these occasions, he complained of persistence of symptoms. He stated that the symptoms had not been relieved by food or bicarbonate of soda. Roentgenologic examination of the stomach revealed a properly functioning gastroenteric stoma and there was no evidence of ulceration.

CASE 6.—A woman, aged 52 years, of Scotch descent, had suffered from pain in the epigastrium and left costal margin for four years. The severity of the pain had increased when the patient had lain down; the pain had not related to the ingestion of food except that there was marked intolerance to fat. She also complained of attacks of colicky pain which was situated in the upper part of the abdomen and extended upward to the left side of the thorax. Nausea and vomiting also had been present. An attack which had occurred one month before the patient came to the clinic had been associated with jaundice, pruritus, chills, fever, and acholic stools. There also had been an attack of "bloody" diarrhea. It was believed that the patient had cholecystitis with cholelithiasis. Cholecystography revealed a nonfunctioning gall bladder. Operation disclosed absence of the gall bladder. The common bile duct was normal and no stones were palpable. The liver was normal but chronic pancreatitis was present. No other operative procedure was employed.

CASE 7.—The patient was a man, aged 57 years, who was a Canadian. For twelve years he had had attacks of colic in the right upper quadrant of the abdomen and morphine had been required to relieve the pain. The attacks had been associated with nausea, vomiting, chills, fever, and mild jaundice. Six months previous to his registration at the clinic he had noticed the pain in the left upper quadrant and the development of a mass in that region. Roentgenologic examination revealed a mass attached to the stomach. The colon was normal. Exploratory laparotomy revealed a lymphosarcoma of the stomach and absence of the gall bladder and cystic duct. The gall bladder fossa in the liver was present. The common bile duct, liver, and pancreas were normal. The malignant lesion was not removed. The patient died eleven months later.

CASE 8.—A man, aged 74 years, of English descent, was found to have no gall bladder at necropsy. In 1918, he had had persistent, severe backache. In 1924, he had complained of severe epigastric distress. A diagnosis of diabetes had been made and a tentative diagnosis of hemochromatosis had been verified by skin biopsy. Examination had disclosed splenomegaly and an enlarged liver. Roentgenologic examination of the stomach had not disclosed any abnormality. In 1926, he came to the clinic because of periumbilical pain of recent origin. His appendix was removed because of subacute appendicitis. He continued to complain of pain in the upper part of the abdomen. He died in 1940 of diabetes, and necropsy disclosed absence of the gall bladder. The liver and pancreas were normal and there was no evidence of bronzing. The gall bladder fossa also was absent. The common bile duct was normal and no stones were present.

CASE 9.—A man, aged 38 years, of Danish descent, at necropsy was found to have no gall bladder. He registered at the clinic because of progressive weakness and loss of strength. The symptoms were too involved to permit one to judge whether they were referable to the biliary tract. Necropsy disclosed miliary tuberculosis, ileal tuberculosis, tuberculous lymphadenitis, tuberculosis of the left suprarenal gland, bronchopneumonia, pernicious anemia, and left hydrothorax. The common bile duct was normal but the cystic duct was absent. The liver and pancreas were normal.

CASE 10.*—A woman, aged 50 years, of Finnish descent, had had attacks of pain in the epigastrium which had been associated with jaundice, pruritus, acholic stools, choluria, and dietary intolerance to fat. Morphine had been required for relief of pain. She also had had symptoms of hyperthyroidism. Palpation revealed a nodular enlargement of the thyroid gland. The basal metabolic rate was +32 per cent. There was tenderness in the epigastrium, and icterus was noticed.

*This is the most recent case that has been observed at the clinic.

Cholecystography did not disclose any gall bladder. Thyroidectomy was performed. Pathologic examination disclosed parenchymatous hypertrophy of degenerating fetal adenomas in a colloid thyroid gland. Two months later exploratory laparotomy disclosed absence of the gall bladder and the cystic duct. There was marked distortion of the second and third portions of the duodenum. The common bile duct was located with difficulty and was situated somewhat posteriorly to the usual site. It was thickened and dilated one and one-half times its normal diameter. No stones were found. There was no gall bladder fossa in the liver but hepatitis, grade 2, and pancreatitis were observed. A T tube was inserted in the common bile duct to be left for more than eight months. Choledochography revealed normal filling of the biliary tree with fine branches. The opaque medium soon was emptied freely into the duodenum.

COMMENT

The symptoms observed in these cases are quite representative of those described in the cases reported in the literature. In many cases they are indistinguishable from the symptoms of cholecystitis. This brings up an interesting thought. The difficulty in judging the pathologic status of the gall bladder from the symptoms in cholecystitis proper has been stressed repeatedly and explained by various theories. Too often, because of the frequent presence of stones in cases of cholecystitis, one tends to accept the simple, easily visualized explanation associating calculous obstruction of the cystic or common bile duct with colic. This path is sometimes misleading and one may encounter, on one hand, a distended hydropic gall bladder after an empyema due to an impacted cystic duct stone in a case in which there is no history of colic, or acute cholecystitis with gangrene and impending perforation and in which the symptoms have largely subsided. On the other hand, in cases in which patients complain of severe colic there may be few findings in the gall bladder and no stones. Without appearing to draw too many conclusions from a rare anomaly, we would like to suggest that the symptoms of cholecystitis may frequently be a reflection of a process going on in the common bile duct or its sphincter rather than in the gall bladder. If this be true, subsidence of symptoms associated with improvement in the common bile duct or its sphincter might occur while the disease in the vesicle can go on to gangrene and perforation. Evaluation of this suggestion would be difficult because of the rarity of the opportunity to get sections of the common bile duct and its sphincter during this stage of cholecystitis.

In four of our cases the patients complained of pain which extended to the left side of the thorax and subscapular region. This is not usual in cases of acute or chronic cholecystitis but has been described from time to time as referred pain in disease of the common bile duct. In none of the cases of congenital absence of the gall bladder has the anomaly been suspected preoperatively as there is no point of distinction from cholecystic disease with a nonfunctioning gall bladder on roentgenologic examination. As competent surgeons easily can overlook an unusually placed gall bladder, failure to find it during

laparotomy is less convincing than is the discovery of this anomaly at necropsy. In order to make certain that the gall bladder is not present, the common bile duct must be identified throughout its entire length. If a T tube is inserted into the common bile duct and if a choledochogram is made, either in the course of or after operation, the possibility of an intrahepatic gall bladder may be eliminated. If the appendix previously has been removed by a sufficiently large incision, there is a possibility that the gall bladder also may have been removed without the knowledge of the patient. A small nubbin at the site of the gall bladder occasionally may be the result of repeated inflammatory episodes.

Interesting speculation is stimulated by the cases reviewed here. Although congenital absence of the gall bladder is rare, the state of the extrahepatic biliary tract is comparable physiologically with the postcholecystectomy state. It offers, so to speak, a naturally occurring opportunity to study the effect of absence of the gall bladder. In 58 per cent of the cases of congenital absence of the gall bladder reported since 1900, the patients have had symptoms suggestive of cholecystic disease with a slight variation in that the pain occasionally extended to the left subscapular region. Forty-eight per cent of the patients had jaundice. In 27 per cent of the cases there were stones in the common bile duct. If one limits the discussion to cases in which the patients were more than 45 years of age, symptoms were present in 73 per cent of the cases. This high incidence of symptoms in the cases reported suggests the existence of some defect in the dynamics of the biliary tract. Doubt is cast on this by the high incidence of cases in which complete relief follows cholecystectomy. Critical evaluation of the situation reveals some similarity to the clinical picture of so-called postcholecystectomy syndrome. The discussions that have marked this postoperative difficulty are applicable here.[27-29] The problem brings up theories of the dynamics of the biliary tract, spasm of the sphincter of Oddi, disturbed rhythmic function of the sphincter, the normal intermittence of biliary flow, the effects of pancreatitis and cholangitis, and the "tension bulb effect" of the gall bladder. A mechanical analogy to the last effect may be found in the mouth blowpipe used in chemistry. The skilled operator distends his cheeks as widely as possible while blowing through the tapering tube. This permits a steady flow of air through the pin-point tip of the tube for long periods of time while the operator breathes comfortably. The rhythmic bellowslike action of the lungs keeps the reservoir in the distended cheeks full. It is possible that in this manner the gall bladder acts as a pump reservoir and prevents a sudden fall of pressure in the biliary tract (and in some cases the pancreatic ducts) on opening of the sphincter of Oddi. This would help the sphincteric action in the prevention of regurgitation of the duodenal contents and help to adjust the pressure in the biliary tract to that of the pancreatic ducts when necessary by

changes in the size of the gall bladder. Giordano and Mann[30, 31] have shown that, in animals which do not have a gall bladder, bile is expressed from the sphincter in an intermittent trickle while in species with a gall bladder the bile is expressed in spurts at the proper stimulus.

To what extent, if any, the common bile duct, hepatic ducts, or intrahepatic bile ducts take over some of the functions of the gall bladder is a moot point. Cox[32] has shown that in rats, which never have a gall bladder, ligation of the common bile duct mechanically produces the changes in the parietal sacculi which generally are accepted as evidence that the hepatic ducts have taken over the function of the gall bladder. In the wall of the duct, which is made up of fibroelastic tissue, there is little muscle. The common bile duct was dilated in nineteen, or 32 per cent, of the sixty cases. In nine of the nineteen cases in which the duct was dilated, stones were present. With the gall bladder absent, it is possible that stasis of the contents of the biliary tract is greater than it is when the gall bladder is present. At any rate, it appears that congenital absence of the gall bladder is a distinct disadvantage. Jaundice was present in 48 per cent of the cases; in 21 per cent of the cases the jaundice was not associated with stones. Stones were present in 27 per cent of the cases, pancreatitis in 18 per cent, and hepatitis in 8 per cent (on gross examination). The clinical picture certainly warrants the assumption that disease of the biliary tract is more common in cases of congenital absence of the gall bladder than it is in cases in which the gall bladder is present, especially in cases in which the patients are 45 or more years of age. Proponents of reflux theories would find fertile soil here. In one case, pancreatitis of the acute hemorrhagic necrotic variety was found.[33] It has been pointed out repeatedly that cholecystitis is a disease of the biliary tract which finds its most prominent manifestation in the gall bladder. The next point of least resistance is the cystic duct, and at times the disease may be found there with a relatively normal fundus.[34] In the absence of the gall bladder and cystic duct the remaining portion of the biliary tract will reflect the disease, be it inflammatory, mechanical, metabolic, chemical, or a combination of all. In an attempt to explain the icterus in cases of jaundice without stone, it is interesting to note that pancreatitis was noted in nine of the thirteen cases and hepatitis in three cases.

In anatomic teaching, it usually is implied that the fossae and impressions on the surface of the liver are produced by pressure of the neighboring organs. Although this seems to be a logical conclusion, in seven cases the fossa for the gall bladder was present in the liver despite the fact there apparently was no gall bladder to create the depression.

Although the number of cases has been, of necessity, small, in ten of the twelve cases of congenital absence of the gall bladder in which

the common bile duct was drained for a prolonged period (three of our cases and nine collected from the literature) complete relief of symptoms was obtained. Similar experience has been obtained in the treatment of "postcholecystectomy syndrome."[35] In one of our cases (Case 2), a T tube was left in the common bile duct for two years despite the fact that there had been no stones or dilatation of the duct. In the four other cases in which symptoms existed, no drainage was employed and the patients continued to complain of the same symptoms. On the basis of this evidence, we advise prolonged drainage of the common bile duct by means of a T tube in cases of congenital absence of the gall bladder in which symptoms are present, even when the common bile duct is of normal size and stones are not found.

SUMMARY

This paper is based on fifty cases of congenital absence of the gall bladder that have been reported since 1900, and on ten cases that have been observed at the clinic. Symptoms resembling those of cholecystic disease were present in 58 per cent of the sixty cases. Forty-eight per cent of the patients had jaundice and 27 per cent had stones in the common bile duct. Symptoms were present in 73 per cent of the cases in which the patients were more than 45 years of age. Prolonged drainage of the common bile duct with a T tube is advocated in the cases in which symptoms are present.

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THE INFLUENCE OF THE LOCAL APPLICATION OF SULFATHIAZOLE ON THE INCIDENCE OF INFECTIONS IN SURGICAL INCISIONS

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NEW forms of sulfonamide drugs with increased bacterial specificity are constantly being developed. Various methods of administration have been used in an attempt to increase their effectiveness. With wound infection still the most common and serious single hazard of surgery, it follows that the surgeon's interest should be directed to the sulfonamide drugs in a quest for the particular form and type of administration best suited to his needs. For this reason it seems only natural that the surgeon's study should turn to the direct application of the sulfonamide drugs to tissues in an attempt to prevent and control infection. Contradictory results and opinions[1-3] have been published recently regarding the efficacy of this method. Part of this controversy arises because the authors fail to make clear whether or not they are treating tissues already infected or tissues merely contaminated with bacteria and therefore sites of potential infection. Meleney and his associates[3] have published the most recent and exhaustive study yet made in man of the value of the direct application of the sulfonamide drugs to what they termed contaminated wounds. They divided the patients used for controls and those treated with sulfonamides into groups based on the amount of tissue damage and the degree of bacterial contamination present in the wounds at the time of treatment. They concluded from this study that the local application of sulfonamide drugs to contaminated wounds will not reduce the incidence of infection in such wounds. They regarded the wounds being treated as contaminated wounds, but they stated that the cases were divided into two groups, one group in which the wounds were treated within three hours and the other in which they were treated after three hours, from the time of the accident. It would seem that in this latter group some of the wounds would be truly infected wounds, not merely contaminated. It is significant to note that in the discussion of this paper, Lockwood, one of the collaborators, pointed out that their conclusion did not mean that on the battlefield the direct application of the sulfonamide drugs to contaminated but not yet infected wounds was of no value. He believed the sulfonamide drugs should be used on such emergency occasions on the battlefield to prevent the multiplication of organisms while casualties await further treatment.

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This present paper deals with the possibility of preventing wound infections in clean surgical incisions, by the application of sulfonamide drugs to such incisions before there is opportunity for contamination to occur. The clear division of wounds into (1) those in which infection is established, (2) those in which contamination is already present before the sulfonamide drugs are applied, and (3) those in which the contamination occurs after the application of the sulfonamide drugs, should be kept in mind, and results of the treatment of these three groups of wounds should not be confused.

The present study was undertaken because of the frequent and serious infections which develop in the incisions made for lobectomies and pneumonectomies. When a number of such incisions had been treated by the direct application of sulfathiazole before contamination of the incision had occurred, the results appeared of sufficient interest to compare with those following similar incisions not treated with any sulfonamide drug. The only cases available for comparison were an equal number of patients in whom lobectomies or pneumonectomies had been done in the period immediately preceding that in which sulfathiazole was employed. Aside from the application of sulfathiazole to the incisions in the one group there are also some minor differences in the treatment used in these two series of cases which will be discussed fully in their proper place, but these are not of sufficient importance to preclude a comparison of the results in these two groups.

MATERIAL AND METHODS

Seventy incisions for lobectomies* and pneumonectomies† were studied. The incisions in all but one‡ case were curving incisions just below the scapula, approximately over the fifth or sixth interspace, extending from close to the midline posteriorly to just beyond the anterior axillary line anteriorly and measuring from 30 to 35 cm. in length. The incisions passed through the skin and subcutaneous tissue, and posteriorly through the trapezius and rhomboid muscles, anteriorly through the latissimus dorsi and serratus anterior. The control or prior group consisted of thirty-five patients. The age of these patients ranged from 9 to 52 years, the average age being 31. The experimental group consisted of the thirty-five patients operated upon in the period immediately following that in which the control group of patients came to operation. The age of these patients ranged from 11 to 57 years of age, the average being 32. In the incisions of this experimental group *not more than 2 Gm.* of sterilized sulfathiazole powder were rubbed into every nook and cranny of these extensive incisions *before* opening into the pleural cavity, thus producing a film of serum and blood saturated

*Lobectomy refers to the removal of individual lobes.
†Pneumonectomy refers to the removal of a complete lung.
‡A shorter anterior incision was used.

with sulfathiazole overlying all of the exposed tissue. The lung lesions for which lobectomy or pneumonectomy were done in both groups of cases are set forth in Table I. From this table and the preceding para-

TABLE I

FREQUENCY OF INCISIONAL INFECTIONS IN RELATION TO THE LUNG LESIONS FOR WHICH LOBECTOMY AND PNEUMONECTOMY WERE DONE IN BOTH CONTROL AND EXPERIMENTAL GROUPS

LESION	UNTREATED WOUNDS			TREATED WOUNDS		
	NO. OF CASES	NO. OF WOUNDS INFECTED	PER CENT OF WOUNDS INFECTED	NO. OF CASES	NO. OF WOUNDS INFECTED	PER CENT OF WOUNDS INFECTED
Carcinoma	3	1	33.3	4		
Bronchiectasis	15	4	33.3	17	3	17.6
Lung abscess	10	7	70.0	8	1	12.5
Tuberculosis	3	0		3		
Cystic disease	3	1		0		
Hemoptysis	1	0		1		
Bronchial stricture	0	0		1		
Neurogenic sarcoma	0	0		1		
Total	35	13	37.1	35	4	11.5

graph the two series are seen to form closely comparable groups of cases both from the point of view of age and the pulmonary lesions for which the operations were undertaken.

RESULTS

The results of treatment of the wounds with sulfathiazole as compared with treatment omitting the direct application of any sulfonamide compound to the wounds is set forth in Tables I and II, the former

TABLE II

FREQUENCY OF INCISIONAL INFECTION IN TWENTY-FIVE CASES OF LUNG ABSCESS AND BRONCHIECTASIS FROM BOTH THE CONTROL AND EXPERIMENTAL GROUPS

LESION	UNTREATED WOUNDS			TREATED WOUNDS		
	NO. OF CASES	NO. OF WOUNDS INFECTED	PER CENT OF WOUNDS INFECTED	NO. OF CASES	NO. OF WOUNDS INFECTED	PER CENT OF WOUNDS INFECTED
Lung abscess	10	7	70.0	8	1	17.6
Bronchiectasis	15	5	33.3	17	3	12.5
Total	25	12	48.0	25	4	16.0

group being referred to as treated wounds and the latter as untreated wounds. Among the thirty-five cases of the untreated control group, thirteen wound infections occurred, an incidence of 37.1 per cent. It is of importance to note that all of these infections were serious, usually developing a definite abscess and spreading cellulitis of the chest wall requiring either simple opening of the incision or more radical surgical drainage. The organisms from these infected wounds varied from pure cultures of *Streptococcus hemolyticus, Staphylococcus aureus,* and *Streptococcus viridans* to the typical mixed flora found in infected

lungs. Eleven of these infections developed between the sixth and tenth days postoperatively, while one occurred twelve days and another seventeen days postoperatively. Twelve of these wound infections developed in cases where operation was carried out for the excision of grossly infected lungs. Four of these latter were cases of bronchiectasis, seven were cases of lung abscess, and one was a case of congenital cystic disease of the lung. The remaining infected wound occurred in a patient with a bronchogenic carcinoma. In nine of these patients with infected wounds, empyemas developed. It is not possible from the available data to determine how often this serious complication was secondary to the infected wound, but in a few of these cases which came under my own observation, it was seen that when a patient who suffered from a wound infection coughed, bubbles of air and pus were forced out of the incision in the expiratory phase and during the inspiratory phase this pus was sucked back into the pleural cavity. In these patients sterile pleural effusions were present before the clinical detection of the infected wounds.

In the thirty-five cases of the treated or experimental group, four wound infections occurred, an incidence of 11.5 per cent. Three of the wound infections were slight. One occurred at the end of six days; culture yielded a pure growth of *Streptococcus hemolyticus* and empyema followed the wound infection. Two of the wound infections occurred three weeks after the operation, at a time when the wounds were apparently well healed. The same peculiar features occurred in both cases. Within the course of a few days the epithelium thinned out, the incision broadened at many points along the wound and finally broke down, producing multiple superficial ulcerations which yielded a culture of *Staphylococcus aureus* in the one case and mixed organisms in the other. Five weeks later there occurred in one of these cases a clinically detectable empyema. The remaining case of wound infection in the experimental series was extensive, characterized by a copious serosanguineous exudate associated with mild infection. Empyema also developed in this patient.

It is interesting to note that in both series the majority of infections developed in cases where operation was performed in the presence of grossly infected lung tissue. This is clearly shown in Table II. In the control group, twelve of the infected wounds occurred in a total of twenty-five cases of bronchiectasis or lung abscess, an incidence of 48 per cent, while in the experimental group in an equal number of similar cases wound infections developed in only four, an incidence of 16 per cent.

DISCUSSION

These results strongly suggest that sulfathiazole powder rubbed carefully into a recent clean operative incision will decrease the incidence and severity of wound infection that might otherwise have developed

from bacterial contamination occurring later in the course of the operation. However, there are some differences in the treatment between the two groups of cases which must be considered before accurate conclusions can be drawn from the results presented in this paper.

Some difference existed in the method of closing the chest, in the two series. In the control series, twenty of the chests were treated by closed drainage* following operation, while the remaining fifteen patients were treated by complete closure† of the chest. This latter method was used in thirty-two cases of the experimental series. It might be felt that this difference in treatment could account for the increased incidence of infection in the wounds of the control group. However, an analysis of the control group shows that five wound infections developed in the fifteen cases in which the chests were completely closed, an incidence of 33.3 per cent, while among the twenty cases treated by closed drainage, wound infection developed in eight, an incidence of 40 per cent. These results appear to indicate that the difference in the method of closing the chest was not an important factor influencing the development of wound infections in these patients.

In the two groups of cases under consideration there was some difference in the technique of removing the lung. In those treated, all the pneumonectomies and all except one of the lobectomies were done by the dissection method. In this method, dissection of individual structures and separate ligation of these structures close to the lung hilus was carried out and the main bronchus of the lobe was cut as far proximally as possible. In the control series, nineteen of the operations were done by this same method but fourteen lobectomies were done by the tourniquet method.‡ Here the lobe to be removed was freed until a tourniquet could be passed about a small pedicle of lung tissue, including its bronchi and blood vessels. The lung was cut distal to the tourniquet, and the pedicle of lung tissue oversewn before the tourniquet was released. In all patient where a lobectomy was done by the tourniquet method, closed drainage of the pleural cavity was carried out. A good deal of unavoidable bacterial contamination of the pleural cavity and wound must result during removal of lung tissue by the tourniquet method. However, the incidence of wound infection in the fourteen cases in which the tourniquet method was employed in the control series was only 28.5 per cent. This is less than the incidence of infected incisions in the total control group.

It is also interesting to note that in the control series there are fifteen cases in which the dissection technique of removal of the lung and complete closure of the chest were done. These fifteen cases compare identically in these respects with thirty-four cases of the experimental

*Refers to an airtight fitting tube into the pleural cavity with the other end under fluid below the bed level.

†Refers to complete closure of the operative incision with no provision made for draining the pleural cavity.

‡All of these chests were drained.

group. Among these fifteen cases in the control group the incidence of wound infection was 33.3 per cent as compared to an incidence of 11.5 per cent in the experimental group.

The development of wound infection must depend largely on the degree of contamination of these incisions, which in turn depends to a great extent on the infection in the lung. The most severely infected lungs are those of bronchiectasis, lung abscesses, and congenital cystic disease of the lung. In the prior group all but one of the wound infections occurred in cases of lung abscess or bronchiectasis, while in the experimental group all of the wound infections occurred in similar cases. In the untreated group there were seven wound infections in ten cases of lung abscess, and five wound infections in fifteen cases of bronchiectasis. In the experimental series, there was one wound infection in eight cases of lung abscess, and three wound infections in seventeen cases of bronchiectasis. These figures are shown well in Table II and it is significant to note that in the group of cases of lung abscess or bronchiectasis in the control series, the incidence of wound infection in twenty-five cases is 48 per cent, while in an equal number of similar cases in the experimental groups the incidence of wound infections is only 16 per cent. However, the greatest difference in the incidence of wound infection is among the cases of lung abscess where 70 per cent of the wounds were infected in the control group and only 17 per cent in the experimental group. In these cases of lung abscess, aside from the local application of sulfathiazole in the experimental group, no difference in the operative technique existed between the two groups which might account for this great difference in the incidence of wound infection.

The method of the general administration of sulfonamide drugs differed between the two groups of patients studied. In the control series, sulfonamide drugs when administered, were most often given within twenty-four to forty-eight hours after operation and by mouth, while in the experimental group all but nine of the patients received sulfathiazole intravenously on the day of operation. Six of the wound infections developing in the control series were in patients who received some sulfonamide compound by mouth within twenty-four hours after operation, while the four wound infections occurring in the experimental series occurred in patients who received sulfathiazole intravenously on the day of operation.

Blood loss was treated in both groups of patients by transfusions of adequate amounts of whole blood during and after operation. While some details of postoperative care varied from time to time, there were no significant differences in this respect between the control and experimental group. It is scarcely possible to consider variation of general resistance to infection among the different patients.

From this analysis it appears that the only factor influencing the different incidence of wound infection in the two groups of incisions

compared in this study was the careful application to the wounds in the experimental group of sterilized sulfathiazole powder before opening into the pleural cavity. In order to determine if the different incidence of wound infection in these two groups could arise merely from chance difference, the figures from the two groups of cases were subjected to a statistical analysis according to accepted statistical methods as described by Hill[4] and Campbell.[5] This analysis demonstrated that the differences in the results between the experimental and control groups and the differences between the subdivisions of groups of cases of bronchiectasis and lung abscess were all statistically significant.

In view of the mixed flora present in infected lungs, the local application of sulfathiazole in the prevention of wound infections in the experimental group would seem to indicate activity against a wide variety of organisms. In vivo and in vitro studies point to the fact that the bacteriostatic effect of the sulfonamide drugs is against a large number of organisms.[6, 7] Possibly many of the wound infections that develop in cases of this type are of a symbiotic nature, and bacteriostatic action against one type of organism is all that is necessary to prevent the development of infection.

Regardless of the exact mode of action of the sulfonamide drugs, the patient's own defenses play the final rôle in the prevention of wound infection. Suppression by the sulfathiazole of the activity and multiplication of bacteria prevents rapid destruction of the patient's tissues and allows the individual's general antibacterial and local inflammatory defenses to come into action before active and definite infection has occurred. It would appear that this well-developed local inflammatory response would be much more effective in destroying a few bacteria present in the wound, than could be possible if infection were well established and causing destruction of tissues before the inflammatory reaction had reached its height.

A study of two of the wound infections in the experimental group is most enlightening in an attempt to understand the effect of sulfathiazole as used in this group of patients. Both wounds were apparently well healed and completely epithelized. Three weeks after operation there was a slow widening of the incision at many points, finally resulting in multiple superficial ulcerations. In one case the organisms cultured were *Staphylococcus aureus* and in the other a mixed flora was found. It was apparent that organisms lying throughout the whole length of these wounds had remained relatively dormant for three weeks. Then, due to unknown factors, their relative virulence increased to a point where they were able to produce active infection. *In spite of this apparent masking of wound infection it is important to point out that these infections were slight compared to any of the wound infections that developed in the control series and especially insignificant compared to some of the large abscesses occurring in the control series.* It also seems worthy of note that these infections occurred at a time

when the deeper structures would be well healed, and therefore penetration into the pleural cavities would not be as likely to occur as in the infections occurring in the control group around the sixth to eighth day after operation.

Numerous objections have been raised to the local application of sulfathiazole to wounds. One of these objections is that it delays healing. This seems unimportant if its use prevents the mortality and morbidity arising from wound infection. In the experimental group, the sutures were removed between the sixth and eighth day and all except one of the wounds appeared well healed. Others suggest that all of the advantages of the direct application of sulfathiazole can be accomplished by the intravenous use of the drug but this is not substantiated in the present study. Moreover, while idiosyncrasies and sensitivities to the sulfonamide drugs do occur,[8-12] serious reactions are encountered more often when these drugs are given by mouth or intravenously. In patients who are sensitive to the sulfonamides, the local application of these drugs may result in a local reaction of hyperemia, serous exudation, and delayed healing, and may well form the basis for one of the infections in the experimental group which showed only mild infection but a copious serous exudate. The recent intradermal test for sensitivity to the sulfonamide drugs developed by Leftwick[13] could be used preoperatively to exclude such individuals in whom the local use of sulfathiazole would be contraindicated. In spite of these objections the logic of the local use of sulfathiazole over other methods of administration for the prevention of wound infections under the conditions in this study is apparent when we consider that the direct application of sulfathiazole accomplishes the maximum concentration of the drug at the most effective place and at the optimum time, with a minimum dose.

It should be stated here that the use of sulfathiazole as carried out in the experimental group is no substitute for careful surgery. However, in spite of all precautions some operative procedures cannot be done without producing some contamination of the incision.

All of the facts presented suggest that sulfathiazole applied to recent sterile operative incisions tends to decrease the severity and reduce the incidence of infection which might otherwise be expected to occur in such wounds as a result of subsequent unavoidable bacterial contamination. Ever since Lister's attempt to produce antiseptic surgical technique, surgeons have continuously sought for a technique to prevent organisms from getting into wounds and establishing infection. The evidence in this paper indicates that the method described accomplishes this to a large degree in certain types of wounds by destruction of contaminating organisms before infection occurs. The facts also suggest the principle that bacteriostatic drugs applied to a wound surface allow the natural defenses of the body to destroy organisms more effectively than these drugs can aid the body in the resolution of an already estab-

lished infection. In order to obtain a true estimate of the value of the local use of sulfathiazole in such operative incisions, further carefully controlled trials of this method of the use of sulfathiazole should be made on a series of alternate patients in whom the operative incisions are subject to unavoidable subsequent contamination. Some situations in which the method might be tried to good advantage are incisions for perforated appendix, perforated peptic ulcer, peritonitis of any origin, empyema, and drainage of a pyonephrosis. Certainly the favorable results reported in this study provide ample justification for further investigation of the method described, and as penicillin becomes available for civilian use, studies along these lines with this new drug may prove fruitful.

SUMMARY

1. Wound infections occurring in thirty-five thoracic incisions for lobectomy and pneumonectomy treated by applying sulfathiazole to the wound before opening the pleura were studied and compared with wound infections in an equal number of similar incision not treated by the local use of sulfathiazole.

2. Thirteen wound infections, an incidence of 37.1 per cent, occurred in the control group, while only four occurred in the experimental group, an incidence of 11.5 per cent. This difference was shown to be statistically significant.

3. All except one of the wound infections in the control group were in cases of bronchiestasis or lung abscess with an incidence of wound infection in these cases of 48 per cent, while in the experimental group all of the wound infections were in cases of lung abscess or bronchiectasis with an incidence of wound infection in these cases of only 16 per cent.

4. After a discussion of other factors which might have accounted for this difference in the frequency of wound infections in these two groups of cases, it was concluded that sulfathiazole applied locally in the experimental series was the only important factor to which the reduced incidence of wound infection in the experimental group could be attributed.

5. Since the publication of Meleney's work[3] there has been a fairly widespread feeling that the topical application of sulfathiazole has no place in surgery. The conditions under which his study was made were entirely different from those of the present study and it seems important that the local use of sulfathiazole should not be abandoned under all circumstances without first considering each situation on its own merits. In consideration of these facts and the favorable results of the present investigation it is suggested that further carefully controlled trials of the use of sulfathiazole by the method described in this paper should be carried out.

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APPENDICITIS AND THE SULFONAMIDE DRUGS

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THE local and the systemic use of the sulfonamide drugs in acute appendicitis has changed the attitude of many surgeons toward several phases of the operative management.

"Where there is pus, drain," "In case of doubt, drain," "The worse they smell, the sooner they're well," and other slogans have been, until recently, potent enough to neutralize any given number of arguments to the contrary. Although well-controlled experimental work and clinical observations for years have established the fact that drains drain only a few hours, and are virtually useless in as diffuse a thing as generalized peritonitis, they are still widely used. The operator who has been confronted previously by pelvic and subphrenic abscesses understandably leans toward any procedure that may forestall their occurrence. Certainly it *seems* good sense to leave a route of egress for any noxious material.

It is significant, then, that in dealing with perforated appendices surgeons, with no qualms, are now closing wounds without drainage. Their readiness to dispense now with drainage will probably still be gratifying to the exponents of the nondrainage technique who have spoken forcefully toward this end for some years with but few converts.

Similarly, but less important, are the changes of attitude regarding the use of silk or cotton suture material in contrast to the more popular catgut. It has become apparent that the use of the less irritating silk or cotton will reduce the number of wound infections while giving a stronger closure. With the advent of the sulfonamide drugs used in the operative field, a few surgeons have been encouraged to use these materials to achieve such benefits.

Inasmuch as the source of this report is a collection of cases from a clinic in which the "no-drainage" and silk techniques have been used extensively, especially prior to the sulfonamide era, by a number of operators, we hope to show just what advantages they afford. In contrast to these studies and as a control, there are the cases of surgeons who during the last eight years uniformly used drains in all instances of peritoneal contamination, and performed the suturing with catgut.

To pick up the thread of the story and to see how these observations developed, we go back about eight years to 1936. In brief, before this time, the appendix was removed through a McBurney incision, catgut

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suture material was used, and the abdomen drained "if necessary." "If necessary" meant if there was either peritoneal contamination or pus evident.

Beginning largely at this time, several surgeon adopted the "no-drainage" technique. The record of their experiences, in the succeeding five years, in (*A*) simple acute appendicitis, (*B*) gangrenous appendicitis, and (*C*) perforated appendices with peritonitis will be discussed in the following paragraphs. All of the cases in this study represent an acute inflammatory process. No instances of subacute, interval, or chronic appendicitis are included.

TABLE I

SURVEY OF 680 CASES OF ACUTE APPENDICITIS WITHOUT GROSS CONTAMINATION OF THE PERITONEAL CAVITY

	NUMBER	SUBSEQUENT WOUND INFECTIONS (%)
No drainage	616	5
Subcutaneous drainage	52	43
Intraperitoneal drainage	12	58

A. SIMPLE ACUTE APPENDICITIS

Certainly it appears that drainage often predisposes to wound infection. The great disparity here suggests that the collection of serum about the folds of the drain provides a medium for the proliferation of bacteria, whereas tight closure may circumvent this.

Subcutaneous Drainage.—The idea of drainage of the subcutaneous tissues alone springs from the hope of *minimizing* wound infections, but there was very little change in their extent as compared with the undrained ones. The total time elapsing from the time of operation until the cessation of drainage showed that those receiving *primary* subcutaneous drainage took, as a rule, several days less to heal finally. On the other hand there were many more of them.

Intraperitoneal Drainage.—At the present there is no common usage of intraperitoneal drainage for simple acute appendicitis. It will be enough, then, simply to point out the increased number of wound infections which followed.

As a whole, Table I reflects what a majority of surgeons have gathered from their own experience, particularly regarding wound infections.

B. GANGRENOUS APPENDICITIS

Gangrenous appendicitis (without perforation) has been separated from simple acute appendicitis in this study for one reason. It has been evident for some time that gangrene of the appendix is associated with heavier bacterial extravasation into the free peritoneal cavity than if gangrene were not present. Thus it should reasonably be expected that more infectious complications would result.

Actually there were positive cultures of the peritoneal fluid at the time of operation in 88 per cent of the gangrenous wounds as contrasted

TABLE II

DATA ON 100 CASES OF GANGRENOUS APPENDICITIS WITHOUT GROSS PERFORATION OR CONTAMINATION OF THE PERITONEUM

	NUMBER	SUBSEQUENT WOUND INFECTIONS (%)
No drainage	70	29
Subcutaneous drainage	25	72
Intraperitoneal drainage	5	100

with 38 per cent in the simple acute type shown in Table I. As a result of this increase in the presence of bacteria, there were 29 per cent wound infections in the group in which drainage was not done, and 72 per cent wound infections in the ones drained subcutaneously. In addition to these wound infections there were three pelvic abscesses, two of which required drainage. One of these two had been drained intraperitoneally and into the pelvis—certainly a suggestion of the inadequacy of drains in preventing deep intra-abdominal abscesses.

Thus far then, we have demonstrated the ability of the peritoneum to resist purely bacterial contamination as well as the distinctly inferior resistance of the abdominal wall tissues. In the latter the infection localizes usually in the poorly vascularized subcutaneous fat while the deeper muscles, with relatively richer blood supply, are less apt to be involved.

C. PERFORATED APPENDICES WITH PERITONITIS

In the case of perforated appendices where there is not only massive bacterial contamination but also varying amounts of particulate matter from within the gut, the resistance of the peritoneum to infection is severely taxed and that of the abdominal wall tissues is usually overwhelmed.

TABLE III

DATA ON 155 CASES OF ACUTE APPENDICITIS WITH PERFORATION AND GROSS CONTAMINATION OF THE PERITONEUM (1936-1941)

	NUMBER	WOUND INFECTION ONLY (%)	% INTRA-ABDOMINAL ABSCESSES (PELVIC AND SUBPHRENIC ABSCESSES, PERSISTENT PERITONITIS)	FATALITIES
No drainage	51	49	28	11.8
Subcutaneous drainage	44	52	32	13.6
Intraperitoneal drainage	60	40	57	23.3

While simple wound infections were quite common in this group, the great difference lies in the type and severity of the infectious sequelae. This is again reflected in the fatality rate of this period (1936 to 1941).

Persistent Peritonitis.—Those patients who had signs of peritonitis (persistent fever, rigid abdomen, no peristalsis) for as much as forty-eight hours after operation are listed in Table IV.

TABLE IV

	NUMBER	PERSISTENT PERITONITIS (%)
No drainage	51	12
Subcutaneous drainage	44	14
Intraperitoneal drainage	60	28

Pelvic Abscesses.—Those developing pelvic abscesses again suggested the failure of drains to really drain. At this time (before the sulfonamide era) evidently an abscess would develop in the pelvis often regardless of whether or not a drain had been inserted there. On several occasions, at subsequent operation, the drain would seem to be satisfactorily draining one pocket, but another near by would have no connection with it.

TABLE V

	NUMBER	PELVIC ABSCESS (%)
No drainage	51	14
Subcutaneous drainage	44	18
Intraperitoneal drainage	60	20

Intestinal Obstruction.—In contrast to the paralytic ileus accompanying peritonitis, mechanical intestinal obstruction occurred occasionally.

TABLE VI

	NUMBER	INTESTINAL OBSTRUCTION (%)
No drainage	51	2
Subcutaneous drainage	44	4.5
Intraperitoneal drainage	60	10.0

As a complicating factor, intestinal obstruction of the mechanical type (usually due in these cases to a kinked loop or adhesions) added greatly to the mortality. It usually appeared from four to ten days after operation. In contradistinction to the ileus of peritonitis there was not a sustained fever, and most important, we feel, there was prominent and persistent hyperperistalsis accompanying the distention. Levin tubes for gastric and duodenal suction often availed but little and at this time (up until 1940) we had not used the Miller-Abbot type of tube.

SILK AND CATGUT

Prior to 1939, catgut was used practically exclusively in all cases of appendicitis. At this time several surgeons began using silk suture material throughout, but limiting the practice to cases of simple acute appendicitis. There was no other change in technique. The results, as compared with the previous 639 cases in which catgut was used, are tabulated in Table VII.

These were not selected cases. We feel that the increased number of wound infections with catgut may be laid to the disintegrating catgut serving as a nidus about which bacteria can proliferate, whereas this reaction about silk may be minimal.

TABLE VII

THE USE OF SILK AND CATGUT SUTURE MATERIAL THROUGHOUT IN ACUTE APPENDICITIS WITHOUT PERFORATION

	NO. OF CASES	WOUND INFECTIONS	PER CENT
Silk	41	1	2.4
Catgut	639	62	9.7

Our original purpose was to extend the use of silk, nylon, and cotton to contaminated wounds and, actually, this was done. However, at this juncture the local use of the sulfonamide drugs came into prominence so the last step in the changing technique reflects both the use of silk suture material and the sulfonamides.

Technique.—Let us recapitulate for a moment on the technique which had thus evolved by 1942. McBurney incisions, no drainage, the use of silk (or nylon or cotton) suture material, and the use of the sulfonamide drugs were fairly well established. To what extent all of the operators adhered to these methods in the next 300 consecutive cases is shown here:

McBurney incisions used in 100 per cent of the cases
Silk suture material used in 96 per cent of the cases
No drainage used in 99.3 per cent of the cases
Sulfonamides used intraperitoneally and in the wound in 97 per cent of the contaminated (perforated) cases; in simple acute appendicitis it was used at the operator's discretion

The results in the last 300 cases have been more than gratifying, first in the remarkably low mortality, and second in the paucity of infectious complications. The entire story is told in Table VIII.

TABLE VIII

RESULTS OF THE LAST 300 CASES OF ACUTE APPENDICITIS

	CASES	INFECTIOUS COMPLICATIONS	DEATHS
Acute	232	2 wound infections	0
Gangrenous	31	1 wound infection	0
Perforated appendices	33	11 wound infections 2 pelvic abscesses 1 subphrenic abscess	1
Abscesses	4 (drainage, catgut)	4 wound infections	0
Overall mortality		0.3%	

Several features of this type of management require some further elaboration.

1. *Wound Infections.*—Wound infections were unusual, and those that occurred did not persist unduly even with silk in the wound. Despite the presence of infection about the appendix at the time of operation, the vast majority heal with no difficulty at all. Those that became infected drained, as near as we could judge, about 50 per cent

longer than the average catgut wound. In our opinion this is a small price to pay for the large number of totally uninfected wounds.

On the other hand, we are offering no statistics on wounds in which *catgut* and the sulfonamide drugs were used, as there were comparatively few of these. Despite the protracted argument over the merits of catgut and of silk, we doubt very much if any life has ever been lost or any great harm done from the use of one suture material over the other. We are here simply emphasizing our own experience with the nonabsorbable sutures which, both before and since the general use of the sulfonamides, have reduced the number of wound infections.

2. *Pelvic Abscesses.*—Of the last 300 cases only two pelvic abscesses were drained. This statement perhaps does not represent the true situation in that at least seven other wounds showed an inflammatory process going on in the pelvis which resorbed with no other therapy than continued administration of the sulfonamide drugs (usually sulfadiazine) by mouth. These pelvic inflammations appeared from the third until the tenth day, and were accompanied by moderate fever, pulse elevation, and leucocytosis. There was a boggy mass palpable per rectum and, somewhat less frequently, tenesmus. However, none was drained, nor was there recurrence of the mass in any.

COMMENT

While this communication was intended to deal mainly with the changes in technique during the last few years, it is only fair to mention one other factor which is also affecting the present picture. This is the obviously earlier diagnosis and operation in appendicitis.

TABLE IX

	PER CENT IN 1934	PER CENT IN 1938	PER CENT IN 1942
Acute	59	71	76
Gangrenous	10	8	10
Perforated	21	16	12
Abscess	10	5	2

The shift away from patients with appendical abscess and peritonitis, and the increase in the simple acute cases need no further elaboration.

SUMMARY

1. A lessening of wound infection and an apparent lowering of mortality were attained when all forms of drainage of the peritoneum and abdominal wall were relinquished. There was no perceptible increase or decrease in the number of intra-abdominal abscesses or in generalized peritonitis.

2. The use of silk suture material reduced the number of wound infections appreciably. Those wounds which *were* infected drained approximately 50 per cent longer than the usual wound in which catgut was used.

3. The use of the sulfonamide drugs locally, used in conjunction with silk suture material and no drainage, has shown remarkable benefits in:

a. Lowering the mortality still further
b. Lessening wound infections
c. Reducing severity of wound infections
d. Lessening the number and severity of intra-abdominal abscesses

4. The use of the sulfonamide drugs and the no-drainage technique has already been accorded general acceptance. The chief purpose of this paper is to accentuate this. The choice of suture material is a factor which plays a lesser role. Our preference is the nonabsorbable suture material, for with it there seems to be a decided lessening of wound infections.

THE PREVENTION OF STAPHYLOCOCCUS INFECTIONS OF THE PERITONEUM

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METHODS of study of infections in animals always entail great difficulty in the control of many factors which influence the course of the infection. Control of the virulence of the organism is only one of the factors which has to do with the creation of infections which are similar in different animals. In studies of the effects of the sulfonamides by many investigators, these variable factors have been controlled in part by the use of large numbers of small animals. Mice are usually used and in most studies microorganisms have been administered intravenously and the various drugs given by mouth. By varying the number of organisms injected and the dose of drug used, the comparative efficacy of the drugs can be assayed with a fair degree of accuracy.

An evaluation of the effect of bacteriostatic agents which are implanted in contaminated wounds is even more difficult. Organisms introduced into wounds of the skin and subcutaneous tissues, or introduced through a needle into the subcutaneous tissues, give rise to widely varying lesions in different animals. This is true even when frozen *Staphylococcus aureus* is used, and in our experience the virulence of this organism, frozen at −78° C., has remained remarkably stable over long periods of time. The effect of the addition of the sulfonamides to such contaminated wounds has, in our hands, been impossible to interpret with exactness. The measurement of the tension required to separate wound edges is of value in the study of the rate of healing of wounds created under exacting "aseptic" conditions. When the many variable factors which influence infections and those concerned with the bacteriostatic effects of the sulfonamides upon bacteria are introduced, the results obtained from such experimental studies as these again become extremely confusing.

It seemed to us that by creating generalized infections of the serous cavities of animals, which were lethal in most instances, the efficacy of various bacteriostatic agents when used locally could be studied to advantage. In a recent publication[1] we reported experiments which tested the local effect of sulfanilamide, sulfathiazole, and sulfadiazine upon the prevention of infection of the pleural cavities of dogs fol-

The sulfadiazine used in this work was supplied by Lederle Laboratories, Inc., New York and E. R. Squibb & Sons, New York.

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The sulfanilamide and sulfathiazole used in this work were supplied by E. R. Squibb & Sons, New York.

TABLE I

CONTROL GROUP: 0.1 C.C. FROZEN SALINE SUSPENSION OF HEMOLYTIC STAPHYLOCOCCUS AUREUS INJECTED

EXP. NO.	DURATION OF LIFE AFTER OPERATION (DAYS)	FINDINGS OF AUTOPSY CAUSE OF DEATH	CULTURE OF PERITONEUM AT AUTOPSY
1	2.5	Generalized peritonitis	H. Staph. aureus
2	4.5	Generalized peritonitis	H. Staph. aureus
3	2.5	Generalized peritonitis	H. Staph. aureus
4	3	Generalized peritonitis	H. Staph. aureus
5	3.5	Generalized peritonitis	H. Staph. aureus
6	6	Generalized peritonitis	H. Staph. aureus
7	3	Generalized peritonitis	H. Staph. aureus
8	6	Generalized peritonitis	H. Staph. aureus
9	3	Generalized peritonitis	H. Staph. aureus
10	2	Generalized peritonitis	H. Staph. aureus
11	3	Generalized peritonitis	H. Staph. aureus
12	1	Pneumonia, peritoneum glistening, no fluid	Sterile
13	3	Generalized peritonitis	H. Staph. aureus
14	1.5	Generalized peritonitis	H. Staph. aureus
15	4.5	Generalized peritonitis	H. Staph. aureus
16	1.5	Generalized peritonitis	H. Staph. aureus
17	3	Generalized peritonitis	H. Staph. aureus
18	2	Generalized peritonitis	H. Staph. aureus
19	2	Generalized peritonitis	H. Staph. aureus
20	3	Generalized peritonitis	H. Staph. aureus
21	2	Generalized peritonitis	H. Staph. aureus
22		Sacrificed, 7 days; peritoneum normal appearance, no fluid	Sterile
23		Sacrificed, 7 days; abscess in omentum, no evidence peritonitis	Sterile
24	6	Generalized peritonitis	H. Staph. aureus
25		Sacrificed 3 weeks; no evidence of infection adhesions +	Sterile

lowing contamination with the hemolytic *Staphylococcus aureus*. Contamination was produced in these animals following total left pneumonectomy.

This report is concerned with a similar series of experiments in which the peritoneal cavities of dogs were contaminated and bacteriostatic agents introduced immediately following introduction of the organism.

METHOD OF STUDY

Dogs which varied rather widely in weight (6 to 18 kg.) were used. In the experiments, care was taken to distribute animals of comparable weights among the control group and the variously treated group.

Attempts to produce generalized peritonitis in a group of animals by injection of organisms into the peritoneal cavity failed. Localized abscesses, or no apparent infection at all, occurred in many animals. The following procedure was suggested by experiments performed by Halsted in studies of infected wounds.[3]

The operative procedure was the same in all experiments and was performed under aseptic conditions. Intravenous nembutal anesthesia

TABLE II

SULFANILAMIDE GROUP: 0.1 C.C. FROZEN SALINE SUSPENSION OF HEMOLYTIC STAPHYLOCOCCUS AUREUS AND 0.3 GM. SULFANILAMIDE PER KILOGRAM BODY WEIGHT

	EXP. NO.	DURATION OF LIFE AFTER OPERATION (DAYS)	FINDINGS AT AUTOPSY, CAUSE OF DEATH	CULTURE OF PERITONEUM AT AUTOPSY
A. Sulfanilamide 0.3 Gm. per kilogram body weight intraperitoneally	26	4	Generalized peritonitis	H. Staph. aureus
	27	2	Generalized peritonitis	H. Staph. aureus
	28		Sacrificed 19 weeks; no evidence of infection, no adhesions	Sterile
	29	21	Generalized peritonitis, many fibrinous adhesions	H. Staph. aureus
	30		Sacrificed 11 weeks; no evidence of infection, adhesions + +	Sterile
	31		Sacrificed 14 weeks; no evidence of infection, no adhesions	Sterile
	32	2	Generalized peritonitis	H. Staph. aureus
	33		Sacrificed 5 weeks; no evidence of infection, adhesions +	Sterile
	34	1	Generalized peritonitis	H. Staph. aureus
	35	3	Generalized peritonitis	H. Staph. aureus
	36	4	Generalized peritonitis	H. Staph. aureus
B. Sulfanilamide 0.3 Gm. per kilogram body weight intraperitoneally and 0.5 Gm. by mouth every eight hours	37		Sacrificed 9 weeks; no evidence of infection, adhesions +	Sterile
	38		Sacrificed 9 weeks; no evidence of infection, no adhesions	Sterile
	39		Sacrificed 7 weeks; no evidence of infection, no adhesions	Sterile
	40		Pneumonia 4 to 5 weeks; no evidence of peritonitis, no adhesions	Sterile
	41	1.5	Generalized peritonitis	H. Staph. aureus
	42		Sacrificed 11 weeks; no evidence of infection, adhesions +	Sterile
	43	4.5	Generalized peritonitis	H. Staph. aureus
	44		Sacrificed 11 weeks; no evidence of infection, no adhesions	Sterile

was administered. A high paramedian incision was made through the abdominal wall. The omentum and spleen were delivered through the wound. The gastrocolic omentum was divided between ligatures near its attachments to the stomach and colon. It was left attached to the splenic pedicle and a ligature of silk was tightly applied at that site. The omentum was in this way completely deprived of its blood supply. A suspension of hemolytic *Staphylococcus aureus,* 0.1 c.c., in normal saline solution was then injected among the loops of intestine. When a drug was used it was introduced immediately after the organism was injected. The omentum was replaced. The peritoneum was closed with a continuous fine silk suture, the fascia and subcutaneous tissues with interrupted

TABLE III

SULFATHIAZOLE GROUP: 0.1 C.C. FROZEN SALINE SUSPENSION OF HEMOLYTIC STAPHYLOCOCCUS AUREUS AND 0.3 GM. SULFATHIAZOLE PER KILOGRAM BODY WEIGHT

	EXP. NO.	DURATION OF LIFE AFTER OPERATION (DAYS)	FINDINGS AT AUTOPSY, CAUSE OF DEATH	CULTURE OF PERITONEUM AT AUTOPSY
A. Sulfathiazole 0.3 Gm. per kilogram body weight intraperitoneally	45	4	Generalized peritonitis	H. Staph. aureus
	46	6	Generalized peritonitis	H. Staph. aureus
	47	4	Generalized peritonitis	H. Staph. aureus
	48	1.5	Generalized peritonitis	H. Staph. aureus
	49		Sacrificed 8 weeks; no evidence of infection, no adhesions	Sterile
	50		Sacrificed 19 weeks; no infection, no adhesions	Sterile
	51		Sacrificed 6 weeks; no evidence of infection, adhesions ++	Sterile
	52	1	Generalized peritonitis	H. Staph. aureus
	53	3.5	Generalized peritonitis	H. Staph. aureus
	54		Sacrificed 2 weeks; infection of abdominal wound, no peritonitis or adhesions	Sterile
	55	4	Generalized peritonitis	H. Staph. aureus
B. Sulfathiazole 0.3 Gm. per kilogram body weight intraperitoneally and 0.5 Gm. by mouth every eight hours	56	2	Hemorrhage from splenic vessel, no evidence of infection	Sterile
	57		Sacrificed 23 weeks; no evidence of infection, no adhesions	Sterile
	58	4	Generalized peritonitis	H. Staph. aureus
	59		Died of pneumonia, 2 days; no evidence of peritonitis	Sterile
	60	1.5	Generalized peritonitis	H. Staph. aureus
	61	3	Generalized peritonitis	H. Staph. aureus
	62	2	Generalized peritonitis	H. Staph. aureus
	63	1.5	Generalized peritonitis	H. Staph. aureus
	64	1	Generalized peritonitis	H. Staph. aureus
	65	1.5	Generalized peritonitis	H. Staph. aureus

fine silk sutures, and the skin with continuous silk. No dressing was applied to the wound.

The saline suspension of the organism was made in large quantity and was placed in Pyrex ampules in amounts of from 1 to 2 c.c. These ampules were placed in containers of alcohol, and frozen in a dry ice chamber at −78° C. Its virulence has been assayed against mice at intervals of time and found to be remarkably stable for as long as eight months. About five billion bacteria were contained in 1 c.c. of the suspension.

More than 100 animals were operated upon. Generally the animals were operated upon in groups of four, six, or eight, control experiments in which no drug was being used being performed with experiments in which the drug was employed. Four types of experiments were performed. In all, 0.1 c.c. of the organism suspension was injected. No

TABLE IV

SULFADIAZINE GROUP: 0.1 C.C. FROZEN SALINE SUSPENSION OF HEMOLYTIC STAPHYLOCOCCUS AUREUS AND 0.3 GM. SULFADIAZINE PER KILOGRAM BODY WEIGHT

	EXP. NO.	DURATION OF LIFE AFTER OPERATION (DAYS)	FINDINGS AT AUTOPSY, CAUSE OF DEATH	CULTURE OF PERITONEUM AT AUTOPSY
A. Sulfadiazine 0.3 Gm. per kilogram body weight intraperitoneally	66	14	Generalized peritonitis	H. Staph. aureus
	67	4.5	Generalized peritonitis	H. Staph. aureus
	68		Sacrificed 8 weeks; no evidence of infection; adhesions ++	Sterile
	69		Sacrificed 8 weeks; no evidence of infection, adhesions ++	Sterile
	70		Sacrificed 10 weeks; no evidence of infection, no adhesions	Sterile
	71	2	Generalized peritonitis	H. Staph. aureus
	72	2.5	Generalized peritonitis	H. Staph. aureus
	73		Sacrificed 6 weeks; abscess of left upper quadrant, no peritonitis	Sterile
	74		Sacrificed 5 weeks; subphrenic abscess, no peritonitis, adhesions +++	Sterile
	75		Sacrificed 5 weeks; no evidence of infection, adhesions +++	Sterile
	76	1	Generalized peritonitis	H. Staph. aureus
	77	1.5	Generalized peritonitis	H. Staph. aureus
B. Sulfadiazine 0.3 Gm. per kilogram body weight intraperitoneally and 0.5 Gm. by mouth every 12 hours	78	8	Generalized peritonitis	H. Staph. aureus
	79	2.5	Generalized peritonitis	H. Staph. aureus
	80		Sacrificed 8 weeks; no evidence of infection, adhesions ++	Sterile
	81	2	Generalized peritonitis	Sterile
	82	4	Generalized peritonitis	H. Staph. aureus
	83	2	Generalized peritonitis	H. Staph. aureus
	84	2	Generalized peritonitis	H. Staph. aureus
	85		Sacrificed 8 weeks; no evidence of infection, adhesions +++	Sterile
	86		Sacrificed 5 weeks; subphrenic abscess, no peritonitis, adhesions +++	Sterile
	87	1	Generalized peritonitis	H. Staph. aureus
	88	1.5	Generalized peritonitis	H. Staph. aureus
	89		Sacrificed 4 weeks; no evidence of infection, no adhesions	Sterile

drug was used in the control experiments. In the other three groups, sulfanilamide, sulfathiazole, and sulfadiazine, respectively were employed. In each experiment 0.3 Gm. of the drug per kilogram of body weight of the animal was the amount used. Coarse crystals of the drug were suspended in about 50 c.c. of sterile distilled water and poured among the loops of small intestine.

About one-half of the animals in each of the groups receiving sulfonamide therapy were also given the drug by mouth, in doses shown in Tables I to VI.

Animals that died less than twenty-four hours after operation are not included in this study.

Samples of blood for determination of the drug concentration were obtained at occasional intervals. The blood concentration determinations were recorded in milligrams per 100 c.c. of blood. Average blood

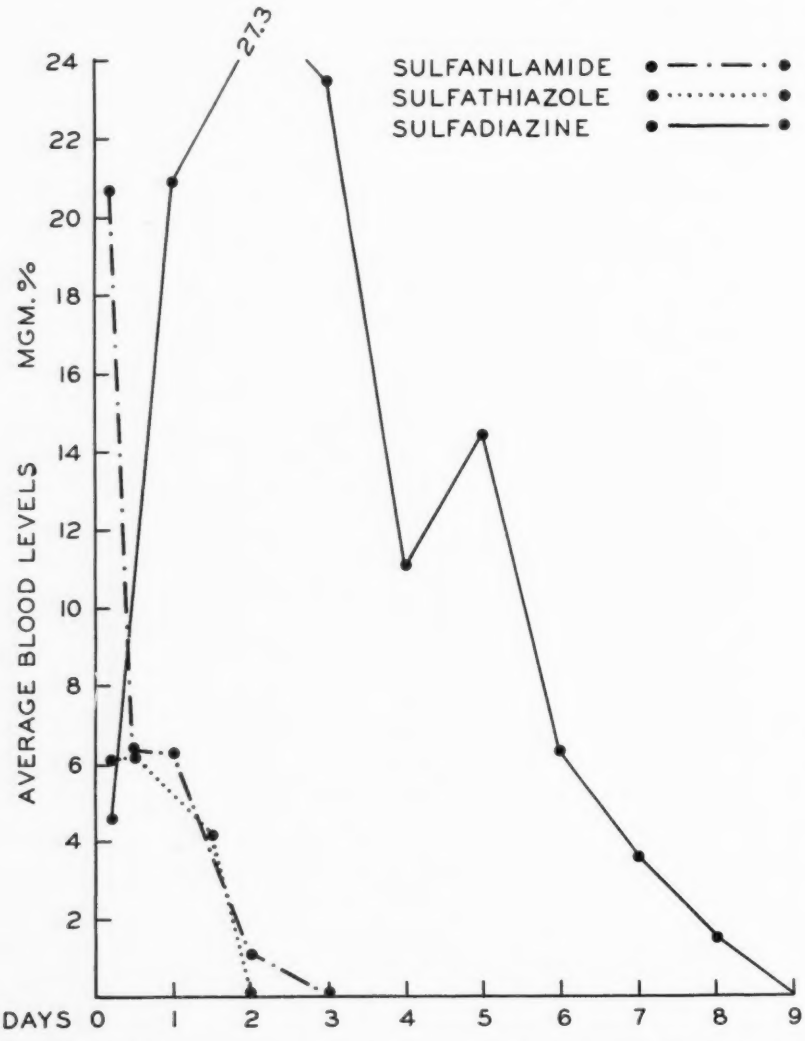

Fig. 1.—Graphic representation of the effects of local implantation of the sulfonamide drugs on blood concentration. Average figures are recorded in milligrams per 100 c.c. of blood.

levels were computed, and the curve of the levels obtained in the experiments in which the drug was administered locally, but not by mouth, is shown in Fig. 1.

Animals that received the drug by mouth were given 0.5 Gm. twice or three times daily. If the animal survived, administration of the drug was continued for ten days. Daily blood levels were recorded, and in all

TABLE V

SUMMARY OF TABLES II, III, AND IV, SHOWING FATE OF SUBGROUPS A AND B IN EACH GROUP

	NUMBER OF DOGS	NUMBER DIED OF PERITONITIS	NUMBER SACRIFICED OR DIED OF OTHER CAUSES	PER CENT DYING OF PERITONITIS	AVERAGE DURATION OF LIFE OF ANIMALS DYING OF PERITONITIS (DAYS)
II (A) Sulfanilamide locally	11	7	4	63.3	5.3
II (B) Sulfanilamide locally, + 0.5 Gm. by mouth every eight hours	8	2	6	25.0	3.0
III (A) Sulfathiazole locally	11	7	4	63.3	3.4
III (B) Sulfathiazole locally + 0.5 Gm. by mouth every eight hours	10	7	3	70.0	2.1
IV (A) Sulfadiazine locally	12	6	6	50.0	4.3
IV (B) Sulfadiazine locally + 0.5 Gm. by mouth every 12 hours	12	8	4	66.7	3.8

TABLE VI

SUMMARY OF FATE OF ENTIRE GROUP OF ANIMALS INOCULATED WITH HEMOLYTIC STAPHYLOCOCCUS AUREUS

	TOTAL NUMBER OF ANIMALS	NUMBER DIED OF PERITONITIS	NUMBER SACRIFICED OR DIED OF OTHER CAUSES	PER CENT DYING OF PERITONITIS	AVERAGE DURATION OF LIFE OF ANIMALS DYING OF PERITONITIS (DAYS)
Control, no drugs used	25	21	4	84.0	3.4
Sulfanilamide group	19	9	10	47.4	4.5
Sulfathiazole group	21	14	7	66.6	2.8
Sulfadiazine group	24	14	10	58.3	4.0

experiments the blood concentration remained high (above 5 mg. per 100 c.c. blood) but varied from day to day.

RESULTS

The effects of sulfanilamide, sulfathiazole, and sulfadiazine on the uncontaminated peritoneum of dogs have been reported by us previously.[2]

The comparative effects of these drugs upon hemolytic *Staphylococcus aureus* infections of the pleural cavity, following pneumonectomy, have also been reported.[1] In the latter article sulfathiazole was found to be more effective in the prevention of empyema in dogs than were the other two drugs. It is surprising, therefore, that fatal peritonitis occurred in a greater percentage of instances in this group of experiments when sulfathiazole was used than when either sulfanilamide or sulfadiazine was used.

The very low mortality rate in the group of animals which received sulfanilamide therapy both locally and by mouth is of interest.

The numbers of animals used in the various subgroups are not great, however, and we believe that one is not justified in the conclusion that any of these drugs is greatly superior to another for the prevention of infections in wounds contaminated with the hemolytic *Staphylococcus aureus.*

The blood concentration curves follow very closely the same form as those obtained with the implantation of sulfanilamide, sulfathiazole, and sulfadiazine in the normal peritoneal cavity. The rate of absorption appears to be slightly prolonged with all three drugs and, as has been previously shown, the rate of excretion of sulfadiazine is much slower than with the other drugs.

Adhesions between loops of small bowel were in general much more numerous and more dense in animals that recovered after sulfadiazine therapy than in those in which sulfanilamide or sulfathiazole was used.

SUMMARY

1. The effects of sulfanilamide, sulfathiazole, and sulfadiazine in the prevention of hemolytic *Staphylococcus aureus* infection of the peritoneum have been studied in the dog.

2. The drugs were applied locally immediately after contamination of the peritoneal surface with carefully measured numbers of the organisms. A number of animals were also given the drug by mouth.

3. Total generalized peritonitis occurred most frequently in the group of animals treated with sulfathiazole and least frequently in those treated with sulfanilamide. The lowest mortality rate in any group occurred in animals treated by means of sulfanilamide given by mouth in addition to local application of the drug.

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CERTAIN SULFONAMIDE DRUGS AND CERTAIN DERIVATIVES OF ASCORBIC ACID IN EXPERIMENTAL GAS GANGRENE IN WOUNDED MICE

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IN TESTING chemotherapeutic agents against gas gangrene in animals a wide variety of assay procedures have been used. Some investigators have induced gas gangrene by the injection of whole cultures of pathogenic clostridia into the muscles of their experimental animals. Others, attempting to simulate the mode of infection of war wounds, have surgically traumatized the muscles and have introduced clostridia into these lesions. The result has been, as Sandusky and Meleney[1] have pointed out, a diversity of opinion on the value of chemotherapy. Likewise, various species of animals have been used as assay organisms. Perhaps the most economical of these is the mouse. The usual procedure in infecting mice has been the injection of whole cultures of clostridia into the thigh. However, in view of the criticisms raised by Sandusky and Meleney we felt it was desirable to develop a procedure for wounding and infecting mice in order to assay compounds against gas gangrene. Our procedure consists in the infection of exposed and crushed thigh muscles and the subsequent treatment of the wound with a powdered drug. The conditions were chosen to obtain under experimental conditions some of the traumatic and temporal characteristics of war wounds.

A number of investigators[2-4] have found that sulfadiazine and sulfathiazole were the most effective of the sulfonamide drugs for the treatment of experimental gas gangrene in mice. Consequently, we have assayed these compounds by our procedure. For comparison with our method of assay we also followed the procedure used by McKee, Hamre, and Rake[4] and injected solutions of sulfonamides, after a previous injection of clostridia and $CaCl_2$, into the unwounded thighs of mice.

It was observed in the course of studies on the nutritional requirements of *Clostridium perfringens* that in vitro growth was inhibited by high concentrations of ascorbic acid. Other investigators[5] have reported success in the use of vitamin C against certain infectious diseases. We therefore also investigated the chemotherapeutic action against gas gangrene of ascorbic acid and some of its derivatives.

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ASSAY PROCEDURE

The culture medium for all strains of clostridia tested contained 0.25 per cent sodium chloride, 0.1 per cent sodium bicarbonate, 0.34 per cent disodium phosphate, 0.082 per cent monopotassium phosphate, 0.5 per cent glucose, 2 per cent Bacto-tryptose, 0.3 per cent Bacto-yeast extract, and 0.1 per cent sodium thioglycolate; pH 7.4. Incubation was at 37° C.

Mice weighing between 20 and 30 Gm. were anesthetized by a subcutaneous injection of nembutal (0.005 c.c. of a solution, containing 25.4 mg. per cubic centimeter of distilled water, per gram of body weight). The extensor muscles of the thigh were exposed by an incision about 5 mm. long, and the appropriate amount of a whole culture of clostridia was injected into the vastus lateralis. The belly of the extensor muscles was then crushed with a fine hemostat for about 3 mm. of its length. After one-half hour about 5 mg. of the compound to be tested were spread into the wound and the incision was closed with a cotton suture. Independent tests showed that the compounds used were not lethal in dosages several times those employed in therapy.

The operation itself was not lethal since all of fourteen mice survived when infection was not attempted. In addition, no deaths occurred in twenty-seven cases where infection was attempted with 0.5 c.c. of old (twenty-four to thirty-hour) cultures of *Clostridium perfringens*.

A six-hour culture of *Clostridium perfringens* in our medium consists of vegetative cells in the logarithmic phase of growth. No spores are formed due to the presence of sugar. When 0.05 c.c. of a six-hour culture of *Clostridium perfringens* (A.T.C.C. No. 846) was injected without subsequent therapy, 100 per cent of eighteen animals died; with 0.03 c.c., 90 per cent of thirty-eight died; with 0.025 c.c., 75 per cent of fifty-nine died. Most of the deaths among infected animals occurred within twenty-four hours and all within forty-eight. Before death the mice exhibited hematuria. The appearance of the dead animals at autopsy was characteristic of the infective organism.[6, 7] Direct smears of the peritoneal fluid of the dead animals showed a predominance of gram-positive perfringens-like organisms.

The deaths were not caused by the culture medium after it had supported the growth of *Clostridium perfringens*. A six-hour culture was filtered through sintered glass under nitrogen. Eight mice survived injection of 0.05 c.c. of this filtrate into their operated thighs. Moreover, all of three animals survived intraperitoneal injections of the same material.

It was possible to kill mice by simply dropping the culture into the incision before the muscles were crushed (that is, without injecting the bacteria into the muscle). However, it was thought that the assay would be more rigorous by admitting bacteria into the connective tissue muscle sheaths. Care was taken to make the operation and infection as constant as possible from experiment to experiment. Nevertheless, there must

have been some variation in the amount of muscle injury and the extent of bacterial invasion.

Other gas gangrene organisms were employed as wound contaminants. When the wounds were infected with *Clostridium septicum* (A.T.C.C. No. 680), *Clostridium histolyticum* (A.T.C.C. No. 6282), or *Clostridium novyi* (A.T.C.C. No. 3540) eighteen-hour cultures were used, while six-hour cultures of *Clostridium sordellii* (Meleney No. 9678) were employed. Between 0.01 and 0.03 c.c. of whole cultures of these organisms was sufficient to kill all of the mice. The appearance of the dead animals upon autopsy was characteristic of the infective organism.[6, 7] Toxins in the culture medium were not responsible for the death of the mice since 0.05 c.c. of sterile filtrates (sintered glass) in each case did not kill any of five mice.

Four different strains of mice were used in these experiments. The CF 1, the C 58, and the P. and S. mice were highly inbred, while the Columbia mice were not genetically homogeneous. In each experiment some mice served as controls and were subjected to the operation and contamination; they were sutured after one-half hour without further treatment. Those in the experimental group received a treatment with the compound indicated. In about 5 per cent of the cases mice failed to recover from the nembutal anesthesia. These animals were, of course, excluded from the experiment.

RESULTS

Table I shows the effect of sulfathiazole and sulfadiazine when applied to wounds infected with *Clostridium perfringens* by our procedure. Sulfathiazole was ineffective in two strains of mice but in the CF 1 strain resulted in a survival that was significantly different from that in the controls (χ^2 test with Yates correction, $P = <0.01$).[8] Sulfadiazine, on the other hand, saved significant numbers of both CF 1 and Columbia mice ($P = 0.04$ and < 0.01, respectively). In many cases large lesions on the thighs of the sulfonamide drug-treated survivors persisted for several weeks until the experiments were terminated.

TABLE I

THE EFFECT OF SULFONAMIDE DRUG POWDER IN WOUNDS OF MICE CONTAMINATED WITH *Clostridium Perfringens*

COMPOUND	SOURCE OF MICE	CONTROLS		EXPERIMENTALS	
		NUMBER OF MICE	PER CENT SURVIVAL	NUMBER OF MICE	PER CENT SURVIVAL
Sulfathiazole	Columbia	16	13	26	19
Sulfathiazole	C 58	10	30	15	20
Sulfathiazole	CF 1	14	0	30	63
Sodium sulfadiazine	Columbia	18	17	36	50
Sodium sulfadiazine	CF 1	15	7	30	67

Results were somewhat different when infection was attempted by the procedure used by McKee, Hamre, and Rake.[4] An injection of

0.05 c.c. of a six-hour culture of *Clostridium perfringens* (a 10^{-1} or 2×10^{-1} dilution in a broth containing the appropriate amount of Ca Cl_2) into the unwounded thighs of Columbia mice was followed after one-half hour by 0.1 c.c. of water containing either 1 mg. of sulfathiazole or 1 mg. of sulfadiazine. Among the sulfathiazole-treated animals 60 per cent of thirty-one mice survived, which was not significantly different from the 53 per cent of the fifteen mice that survived among the controls. However, sulfadiazine resulted in the survival of 97 per cent of thirty mice, which is significantly different from the controls ($P = < 0.01$). Whether the Ca Cl_2 injured the bacteria as well as the muscle into which it was injected is not known.

In Columbia mice infected with *Clostridium perfringens*, l-ascorbic acid resulted in a survival that was statistically different ($P = < 0.01$) from that of the controls (Table II). This was not the case in the other strains of mice. When sodium ascorbate powder was used no significant increase in survival over the controls was obtained. However, ascorbic acid is very labile in neutral solutions. In order to obtain indirect evidence as to whether the effect of l-ascorbic acid was due simply to its acidity, the action of a compound with a similar dissociation constant, succinic acid, was investigated. In two experiments where 25 per cent of eight controls survived, 61 per cent of eighteen treated animals lived. This is not a significant difference ($P = 0.2$), and suggests that ascorbic acid does not work solely by virtue of its acidic properties.

TABLE II

THE EFFECT OF l-ASCORBIC ACID AND SOME DERIVATIVES IN WOUNDS OF MICE CONTAMINATED WITH *Clostridium Perfringens*

COMPOUND	SOURCE OF MICE	CONTROLS		EXPERIMENTALS	
		NUMBER OF MICE	PER CENT SURVIVAL	NUMBER OF MICE	PER CENT SURVIVAL
l-ascorbic acid	Columbia	33	9	60	40
l-ascorbic acid	P. and S.	10	30	24	24
l-ascorbic acid	C 58	9	10	17	11
Sodium ascorbate	Columbia	20	20	35	31
Dehydroascorbic acid	Columbia	8	12	18	0
l-isoascorbic acid	C 58	19	10	30	37
d-glucoascorbic acid	C 58	5	20	10	10

Low concentrations of l-ascorbic acid may produce redox potentials in wounds favorable for the growth of anaerobes.[9] This factor may antagonize the therapeutic action of ascorbic acid and account for the failure of some of the mice to survive after treatment. Hence the action of dehydroascorbic acid was investigated but this compound was not effective. The great lability of dehydroascorbic acid unfortunately makes the result equivocal. Other analogues of ascorbic acid were also tested. No effect was obtained with d-glucoascorbic acid but l-isoascorbic acid resulted in an increased survival among the experimental animals which may be significant ($P = 0.06$).

A few attempts to save infected mice by previous feeding with high concentrations of l-ascorbic acid (1 mg. of neutralized ascorbic acid per day for nine days) failed. Likewise, subcutaneous injection of neutralized solutions of ascorbic acid and injection into the vastus lateralis after contamination were without effect.

TABLE III

THE EFFECT OF SULFONAMIDE DRUGS AND ASCORBIC ACID IN WOUNDS OF COLUMBIA MICE CONTAMINATED WITH WHOLE AND WASHED CULTURES OF *Clostridium Septicum*, *Clostridium Histolyticum*, *Clostridium Novyi*, AND *Clostridium Sordellii*

TREATMENT	ORGANISM							
	SEPTICUM		HISTOLYTICUM		NOVYI		SORDELLII	
	NUMBER OF MICE	PER CENT SURVIVAL	NUMBER OF MICE	PER CENT SURVIVAL	NUMBER OF MICE	PER CENT SURVIVAL	NUMBER OF MICE	PER CENT SURVIVAL
Whole Culture								
Control	5	0	9	0	5	0	5	0
l-Ascorbic acid	9	0	17	12	8	0	10	0
Sulfathiazole	9	22	17	18	9	0	10	10
Sodium sulfadiazine	9	0	17	18	7	0	10	0
Washed Culture								
Control	3	0	5	0	5	0	5	0
l-Ascorbic acid	7	0	10	0	10	0	9	0
Sulfathiazole	9	0	10	0	9	11	10	0
Sodium sulfadiazine	8	0	10	0	10	20	10	0

Some preliminary experiments on the chemotherapy of *Clostridium septicum*, *Clostridium histolyticum*, *Clostridium novyi*, and *Clostridium sordellii* infections in Columbia mice are reported in Table III. Neither l-ascorbic acid, sulfathiazole, nor sulfadiazine, after the injection of whole cultures, resulted in significant increases in survival over the controls. These negative results cannot be due to the presence of toxins in our cultures. In the first place, as mentioned before, sterile filtrates of these cultures were not toxic. To further test this point, cells which were twice resuspended in fresh culture medium, and hence washed free of their metabolic products, were used as contaminants. As Table III shows, the response to therapy remained the same as when whole cultures were used. None of the differences shown in Table III have a P of < 0.2.

DISCUSSION

Perhaps the most interesting conclusion to draw from these results is that the value of chemotherapy depended in some way upon the strain of mice used for the experiment. For example, sulfathiazole and l-ascorbic acid were effective in some strains of mice but not in others. Discrepancies among the results obtained with chemotherapy by other investigators[1] may be accounted for to some extent by differences in the strain of experimental animals used. Sulfadiazine was the only compound investigated which was successful against gas gangrene in

at least two different strains of mice. This result is in accord with the fact that, of the sulfonamide drugs, sulfadiazine has been the most generally effective against experimental gas gangrene in the hands of other investigators.[1-4, 10, 11]

If, however, a drug can be effective in one strain of mice and not another, it is not surprising that results from animal experiments have not predicted with accuracy the results in man. For example, the sulfonamide drugs have been disappointing in the treatment of gas gangrene in World War II.[12] Therefore, the partial success we have obtained by the use of ascorbic acid in mice infected with *Clostridium perfringens* can be, at the most, only suggestive.

Mice are not known to require ascorbic acid in their diet but the therapeutic dose used in the wounds was, gram for gram of body weight, far above the daily nutritional requirement of the guinea pig and man. However, a case of vitamin C hypervitaminosis is unknown.[5] Ascorbic acid has been known to be effective in various ways in the treatment of other infectious diseases,[5] but there is no evidence from our work to describe its mode of action against *Clostridium perfringens.*

SUMMARY

1. A method is described for wounding and infecting mice with various strains of pathogenic clostridia.

2. In two strains of mice the local application of sulfadiazine saved about 60 per cent of the animals infected with *Clostridium perfringens,* a significant difference from the controls.

3. Sulfathiazole was also effective against *Clostridium perfringens* in one strain of mice but not in others.

4. In one strain of mice ascorbic acid saved about 40 per cent of the animals infected with *Clostridium perfringens,* a significant difference from the controls. However, it was ineffective against gas gangrene in other strains.

5. Ascorbic acid, sulfadiazine, and sulfathiazole were ineffective against infections caused by *Clostridium novyi, Clostridium histolyticum, Clostridium sordellii,* and *Clostridium septicum.*

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THE EFFICACY OF HEPARIN ADMINISTERED BY INTRAVENOUS, INTRAMUSCULAR, AND SUBCUTANEOUS ROUTES AND A STUDY OF THE EFFECT OF FIVE BACTERIOSTATIC AGENTS ON HEPARIN ACTION

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THERAPEUTIC administration of heparin to be ideal should result in a prolonged, constant, and controllable elevation of the coagulation time of venous blood. Single intravenous injections result in a marked, but unsustained, rise in coagulation time. Intramuscular injections give a more controllable effect, which is preferable for therapy. The peak of the anticoagulant effect is less extreme and it develops longer after administration. The intramuscular use of heparin has not been widely adopted hitherto because of the high cost. The potentiation of the action of heparin by small doses of dicumarol[2, 7] makes it possible to use the intramuscular route with greater economy.

The response to standard intramuscular injections of heparin has been studied in a group of adults and compared with that of the intravenous and subcutaneous injection of heparin. The local reaction to injected heparin has been studied using heparin in physiologic saline solution as a control and heparin with five different preservatives. Both the local reaction produced and the effectiveness of the preparation in coumarinized and noncoumarinized individuals have been considered. Because of the possibility of contamination, we have preferred not to use heparin without a preservative for routine purposes.

Subcutaneous administration of heparin gives results similar to those obtained with intramuscular administration. However, it gives the patient greater discomfort and there is usually an area of induration and tenderness which persists for twenty-four hours. Heparin is inactive when administered orally.

Two substances, benzidine and protamine, have been found to inhibit the action of heparin when injected coincidentally with heparin.[1, 3] Of the five preservatives studied here, namely phenol, trieresol, merthiolate, phenylmercuric borate, and chlorobutanol, none seemed to have any inhibitory effect in the concentration used.

METHODS

An unselected group of patients with vascular pathology requiring anticoagulant therapy was studied.

We are indebted to the Lederle Laboratories, Inc., Pearl River, N. J., for the heparin preparations tested.

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A given dose of heparin was administered and the coagulation time of venous blood determined by the method of Lee and White[4] at thirty, sixty, ninety, and 120 minutes after the time of injection.

Heparin was injected intravenously in 50 mg. doses in a few cases, but usually in 10 to 20 mg. doses. Intramuscular injections of 50 mg. were made into the gluteus muscles. Subcutaneous injections of 50 mg. were made into the subcutaneous tissue of thigh, flank, abdomen, and back.

Heparin solutions used all contained 10 mg. per milliliter[3] of the sodium salt of heparin. The preservatives used were phenol, 0.5 per cent; chlorobutanol, 0.5 per cent; phenylmercuric borate, 0.004 per cent; merthiolate, 0.01 per cent; and trieresol, 0.3 per cent. Heparin in physiologic saline solution was used as a control.

The local reaction to intramuscular and subcutaneous injection was judged subjectively and objectively. Subjectively, patients were questioned as to soreness immediately upon injection, twelve hours after injection, and twenty-four hours after injection. Objectively, the areas of induration and erythema, if any, were measured at twelve hours and at twenty-four hours. Wherever possible, each patient was given injections with as many different preservatives as possible, both intramuscularly and subcutaneously, at some time in this course of treatment.

RESULTS

Intravenous injection of heparin resulted in a sharp rise in coagulation time within five minutes. An injection of 50 mg. caused an elevation of coagulation time to between 200 and 250 minutes, and an injection of 20 mg. raised the coagulation time to between 100 and 120 minutes. The coagulation time returned to normal within one to two hours.

Intramuscular injection of 50 mg. of heparin caused a slower elevation of coagulation time, and the elevation was less marked than on

TABLE I

COAGULATION TIMES FOLLOWING THE INTRAVENOUS ADMINISTRATION OF HEPARIN

PATIENT	DOSAGE (C.C.)	VENOUS COAGULATION TIME IN MINUTES			
		BEFORE INJECTION	AFTER INJECTION		
		0 MIN.	30 MIN.	60 MIN.	90 MIN.
I. L.	1	15		60	30
J. H.	1	20		65	35
R. J.	1	15	80	45	
S. L.	2	20	180	100	25
A. G.	2	15	125	90	30
A. C.	1	12	85	60	30
W. M.	1	12		80	
G. W.	2	15	110	80	30
M. C.	1	20	110	100	20
Average	1.3	16	115	75.5	28.5

TABLE II

COAGULATION TIME OF VENOUS BLOOD IN MINUTES AFTER INTRAMUSCULAR INJECTION OF 5 C.C. OF HEPARIN

	PATIENT NO.	BEFORE INJECTION	AFTER INJECTION			
			30 MIN.	60 MIN.	90 MIN.	120 MIN.
Heparin in 1/25,000 phenylmercuric borate	21	25	30	45		25
	9	18	32	47	35	
	24	20	37	47	28	
	30	10	42	55		
	30	25	50	60		
	2	20		60	35	
	18	20	35	48	35	
	22	15	35	45		
	Average	19	37	51	33	25
Heparin in physiologic saline solution	15	15	25	35	20	
	16	15				20
	8	15	30	40		30
	14	18	32	42	30	
	4	20	40	50	20	
	29	20	32	45	90	
	7	20	32	50	30	
	2	20		50	35	
	18	20	33	48	35	
	32	15	32	50		
	22	15	35	45		
	Average	17.5	32	45.5	37	25
Heparin in 0.5 per cent phenol	25	18	32	48	20	
	5	10		60		
	6	10		50		
	Average	13	32	53	20	
Heparin in 1/10,000 merthiolate	17	15	33	46	28	
	26	18	35	48		23
	19	16	30	40		21
	27	20	35	45		
	2	20		55	40	
	17	20	35	50	35	
	10	20	25	45		
	32	20	32	50		
	Average	19.5	32	47.0	34	22
Heparin in 0.3 per cent tricresol	22	18	35	50		
Heparin in 0.5 per cent chlorobutanol	21	15	27	45	32	
	31	18	32	45		23
	Average	16.5	28.5	45	32	23

intravenous injection. The coagulation time rose to an average of 32.8 minutes one-half hour after injection and to 47.5 minutes one hour after injection. The coagulation time had returned to normal within two to two and one-half hours after the time of injection.

Subcutaneous injection of 50 mg. of heparin gave essentially the same results as an intramuscular injection.

The presence of the various preservatives in the strengths used seemed to have no demonstrable effect on the action of heparin, for in all cases the elevation of coagulation time was similar to that observed when heparin was used in physiologic saline solution.

Furthermore, the preservatives had no effect on the potentiation of heparin action by dicumarol, for the same degree of potentiation appeared using heparin in physiologic saline solution and heparin with the various preservatives.

The intravenous use of heparin gave no immediate or delayed pain nor any objective sign of reaction in the vein.

The intramuscular injection of heparin in physiologic saline solution and in chlorobutanol caused only a slight aching sensation at the moment of injection and only a slight residual soreness twelve to twenty-four hours after the time of injection. There was no erythema nor induration at the site of injection.

Intramuscular injections of heparin in phenol, phenylmercuric borate, merthiolate, and tricresol were slightly more painful immediately, and resulted in a deep soreness and induration that was marked at the end of twenty-four hours, disappearing in most cases after forty-eight hours. There were four instances of severe local reaction with erythema and edema of one-half the gluteal region persisting for five to seven days after injection. Two of these reactions appeared after heparin was given in phenol and two after heparin in phenylmercuric borate, all four occurring in patients who were fully coumarinized and who had been getting intramuscular gluteal injections of heparin every sixth hour for seven to ten days.

In contrast to these, twelve patients in the present series received heparin in the same dosage while fully coumarinized for periods of twelve to sixteen days without untoward local reaction. The heparin used contained the less irritating preservatives.

TABLE III

COAGULATION TIME OF VENOUS BLOOD IN MINUTES AFTER SUBCUTANEOUS INJECTION OF 5 C.C. OF HEPARIN

	PATIENT NO.	BEFORE INJECTION	AFTER INJECTION			
			30 MIN.	60 MIN.	90 MIN.	120 MIN.
Heparin in 1/10,000 merthiolate	12	18	25	40		25
Heparin in 0.3 per cent tricresol	1	20	32	45	35	
	12	18	28	42		
	1	21	31	45	30	
	Average	19.2	29.0	43	32.5	
Heparin in phenyl-mercuric borate 1/25,000	12	15	25	40		32
	12	18	30	40		28
	1	20	35	45	35	
	Average	17.6	30	41.6	35	30
Heparin in physiologic saline solution	1	20	32	45	35	
	22	18	38	44		
	Average	19	35	44.5	35	
Heparin in 0.5 per cent chlorobutanol	12	15	25	40		25
	1	20	32	42	32	
	Average	17.5	28.5	41	32	25

TABLE IV

COAGULATION TIME OF VENOUS BLOOD AFTER INTRAMUSCULAR INJECTIONS OF 5 C.C. OF HEPARIN

	PATIENT NO.	BEFORE INJECTION (MIN.)	BEFORE COUMARINIZATION 30 MIN.	60 MIN.	90 MIN.	120 MIN.	AFTER COUMARINIZATION BEFORE INJECTION (MIN.)	30 MIN.	60 MIN.	90 MIN.	120 MIN.	PLASMA PROTHROMBIN CONCENTRATION (% OF NORMAL)
Heparin in 0.5 per cent phenol	25	18	32	48	20		18	55	60		42	25
	5	10		45	20		10		55		50	35
	Average	14	32	47	20		14	55	58		46	
Heparin in 1/10,000 merthiolate	17	18	32	47	27		22	50	110	90		20
	26	18	32	48		27	25	60	90		60	20
	19	18	30	40		22	20	55	80		40	30
	Average	18	31	45	27	25	23	55	93	90	50	
Heparin in 1/25,000 phenylmercuric borate	21	15	22	46		25	25	50	90		70	40
	9	18	34	47	35		20	60	90	60		40
	14						22	45	70			45
	31						23	60	90	48		50
	24	20	36	47	28		25	50	100	65		40
	Average	18	32	47	31	25	23	53	88	58	70	
Heparin in physiologic saline solution	15	15	25	30	20		25	45	90	60	35	40
	16						20	60			50	20
	4	20	40	50	20		25	55	90	45		45
	29	20	32	45	30		25	55	90	60		40
	7	20	33	50	30		27	55	90	50		40
	Average	19	32	44	25		24	54	90	54	43	
Heparin in 0.5 per cent chlorobutanol	21	18	32	48		25	25	50	90		70	40

Three patients received intramuscular and subcutaneous heparin daily for periods ranging from two to four months without marked local reaction.

Subcutaneous injection of 50 mg. in physiologic saline solution and in chlorobutanol gave more immediate pain and more tenderness with some induration after twenty-four hours than the same preparations used intramuscularly.

Subcutaneous injection of heparin in phenol, phenylmercuric borate, merthiolate, and tricresol gave severe immediate pain and marked tenderness and induration lasting twenty-four to forty-eight hours after injection.

DISCUSSION

The intravenous use of heparin as a continuous drip can be used to maintain elevation of blood coagulation time,[5, 6] but the method subjects the patient to the inconvenience of a continuous intravenous drip and the coagulability is not easily maintained within the therapeutic range. The coagulation time rises sharply within five minutes after single injections and frequently goes beyond the range which we usually maintain (thirty to forty minutes). The average coagulation time, thirty minutes after the intravenous injection of 10 mg. of heparin, was 115 minutes.

Intramuscular administration of heparin results in a smaller, more manageable alteration of blood coagulability and the simultaneous use of oral dicumarol permits the use of smaller amounts of heparin, making the method economically more practicable. The discomfort caused by four intramuscular injections of heparin spaced over a twenty-four hour period is not excessive and most patients tolerate the procedure well.

The subcutaneous route of heparin administration has no advantage over the intramuscular route as far as the therapeutic action of heparin is concerned. This form of administration is very painful and gives rise to fairly marked local reactions. For these reasons we feel the subcutaneous route is not to be recommended.

Of the five preservatives, phenol, tricresol, phenylmercuric borate, merthiolate, and chlorobutanol, studied in the course of this investigation, chlorobutanol seems to cause the least local reaction and to be the agent of choice. The use of heparin in physiologic saline solution is presumably attended by greater danger of infection because of the lack of bacteriostatic action. None of the five preservatives in the dilutions used caused any alteration of heparin action or of the potentiation of heparin action by oral dicumarol.

CONCLUSIONS

1. Of the three parenteral routes of heparin administration studied, that is, intravenous, intramuscular, and subcutaneous, the route of

choice would seem to be the intramuscular because of a slow, relatively even rate of absorption. This is made more practicable by the coincident oral administration of dicumarol to maintain an effective plasma prothrombin concentration of 20 to 30 per cent of normal, thus reducing the amount of heparin needed to maintain a venous coagulation time of thirty to forty minutes.

2. Of the five preservative agents studied, phenol, 0.5 per cent; trieresol, 0.3 per cent; merthiolate, 0.01 per cent; phenylmercuric borate, 0.004 per cent; and chlorobutanol, 0.5 per cent, the agent of choice for intramuscular injections is chlorobutanol because it produced the least local reaction.

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THE ALLERGIC PATHOGENIC MECHANISM OF THYROTOXICOSIS

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THIS communication will review certain pertinent factual knowledge concerning thyrotoxic disease (such as exophthalmic goiter and Basedow's disease). It will then review the knowledge of thyrotoxic crises as the most convenient method for the study of this disease. Finally, it will attempt the interpretation of the biologic pathogenesis of thyrotoxicosis.

Routine experiences with thyrotoxicosis include the following.

1. The usual type in which there is a gradual development of the disease to its maximum and in which the onset is not acute and does not apparently follow some well-defined incident or event. No crisis-like incident occurs during the course of the illness.

2. Similar types as in Group 1, but in which the onset of the illness is relatively acute and well marked owing to the fact that the disease follows some well-defined incident or event. No crisis-like incident disturbs the course of the illness.

3. A small group in which the illness follows some well-defined incident or event including mental shock, physical injury, etc. The progress of the disease is very rapid so that a fully developed clinical picture is very quickly established. Many of these patients develop extreme grades of exophthalmos. The initial phase of the illness resembles a crisis-like incident.

In one case, encountered many years ago, a woman in her twenties received a sudden great shock. Extreme nervousness occurred immediately, followed by tachycardia, sweating, diarrhea, loss of weight, and exophthalmos. Within a space of days there was a fully developed picture of exophthalmic goiter and the patient went through a typical crisis. She had been in a highly toxic state for more than one year before she was admitted to the hospital. She showed photographs of herself both prior to the beginning of the illness and later, and one could not help being powerfully disturbed at the change from a beautiful, slim girl, with a bright intelligent face, to a gross, fat, drab, old-looking woman, with a high grade of exophthalmos, and with a dull, unintelligent face which was almost repulsive.

4. A group of cases similar to those in Groups 1 and 2, in which for no discoverable cause, and/or with or without some mental or physical provocation, the toxic state of the patient becomes so markedly and comparatively suddenly increased that the patient passes into a crisis from which recovery does not often follow.

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5. A group of thyroidectomies including those done in one or in multiple stages, or patients in whom some relatively trivial operation is done such as polar ligation. In these, following immediately after operation, the patient passes into a crisis. So many of the patients die that this constitutes the greater number of fatalities after operation. While this experience occurs in individuals with a preoperative state of high toxicity, I have seen instances in which the toxicity has been of moderate grade.

The postoperative crises are not necessarily limited to operations upon the thyroid. They are known to occur after other classes of operations and among these, rhinologic procedures possibly take a prominent place.

Cases of allergic rhinitis are relatively common in association with thyrotoxicosis. Flare-ups and crisis-like episodes are especially common after thyroid operations.

6. All of these groups are represented, possibly to a lesser degree, in postoperative recurrences.

7. Cases, sometimes of mild degree, in which following the use of iodine (Lugol's solution), similar exacerbations, even to the intensity of a crisis, occur.

8. Patients with marked mental aberrations and psychologic disturbances in whom thyroid operations are never known to relieve the mental disturbance.

To illustrate, there was one young married woman in whom a severe type of thyrotoxicosis was associated with mental symptoms centered chiefly in an uncontrollable desire to empty the bladder at the most unexpected and inopportune times, so that many times she involuntarily emptied her bladder under conditions which caused much embarrassment. After subtotal thyroidectomy, all of the previous symptoms disappeared except this one which could never be eradicated (six years' follow-up).

The Thyroid Crisis.—

Crises occurring in toxic thyroid disease may develop in any case, including the most unexpected. That thirty-three of forty-nine nonsurgical deaths were due to crisis, as compared with twenty-three of the forty surgical deaths (Boyce[9]) is undoubtedly significant. Most of the nonsurgical deaths from crisis occur in the medical wards, in patients for whom surgery does not seem to have been contemplated.

Patients with toxic thyroid literally stand in jeopardy every hour. This condition is at its maximum immediately after thyroid operations. Patients in which there was no operation are subject to many other stimuli sufficient to throw them into a crisis. The subjects seem not to tolerate the mere act of living. They react badly to psychic trauma and to consequent emotional disturbances. The most trivial intercurrent illness or accident is enough to destroy their delicate balance and to throw them into crises which may readily prove fatal. Similar crises may also result from operations on distant organs and even minor surgical inter-

ventions, roentgen therapy (Bansi[1]), massive thyroid medication, and sudden interruption of a preoperative iodine therapy, infections, diagnostic procedures such as the determination of the basal metabolism, bodily exertion, and severe emotional strains. A severe thyrotoxicosis may also lead spontaneously to a crisis.

All thyroid types of operations—unilateral or bilateral resections of the gland, polar ligations, etc., either in single or multiple stages—carry the danger of a subsequent crisis in almost equal degree. For all surgeons, the relative number of such postoperative crises is to a certain extent a matter of skillful operative technique, of good fortune, and of good and prolonged preparation of the patient before operation. The latter, especially, is a most important factor.

At one of our hospitals I compared the results of operation and the frequency of occurrence of postoperative crises of the operations done in one stage by myself and those done by the other members of the staff who did their operations in multiple stages. I could not see much of any difference in results between the two groups.

The symptoms of the fatal postoperative crisis are characteristic and too well known to require description. Those of the other, the nonpostoperative form, very similarly as the different clinical forms of thyrotoxicosis. Aggravation of existing symptoms is characteristic and those referable to some organic system, such as the gastrointestinal and cerebral systems, predominate.

In severe cases, the patient exhibits increasing muscular atrophy, frequent vomiting, diarrhea which defies treatment, motor unrest, anxiety, sleeplessness, psychotic delusions, and finally coma. There is dryness of the hair and skin. There is a tendency toward descending infection in the respiratory tract, and an increasing malfunction of the cardiovascular system. An increasing amount of urobilinogen is found in the urine with a tendency toward oliguria, and a great increase in creatine in proportion to the total creatinine.

The course of the illness during a crisis may be fatal after one or a few days, or the symptoms may recede after the exciting factor, such as infection, subsides or effective therapy is instituted.

No diagnostic means exists for detecting the impending crisis except in the clinical manifestations of the disease. Not always are these recognizable even to an observant physician. For this reason, every case deserves the utmost care and watchfulness.

1. *Pathogenesis, Pluriglandular Origin.*—Originally it was generally assumed that thyrotoxicosis was essentially a primary disorder of the thyroid. The possibility of the existence of varieties of thyrotoxicosis, in which the primary seat of the disease is outside of the thyroid, has since been recognized, however. Most clinical and research observers have classified the disease according to the assumed probable primary seat of the disorder as follows:

A. Primary thyrotoxicosis, that is, thyrotoxicosis primarily of thyroid origin.

B. Secondary thyrotoxicosis, of which three subvarieties may be recognized:

(a) Those of pituitary origin—thyrotropic hormone excess
(b) Those due to deficiency or antithyrotropic principle
(c) Those of endocrine origin other than pituitary.

The normal activity of the thyroid is dependent upon pituitary secretion. Experimental ablation or destruction of the pituitary gland leads to physiologic and morphologic involution and atrophy of the thyroid.

In many of the cases of crises, post-mortem examination has demonstrated the presence of changes in the posterior lobe of the pituitary (Sunder-Plassmann[54]).

The pace-making thyrotropic factor is derived from the pituitary gland, but the demonstration of an excessive thyrotropic factor in the blood in thyrotoxicosis has so far been unsuccessful, possibly because the secretion is fixed or altered in some way to make it unrecoverable. The culminating factor in thyrotoxicosis is some degree of thyroid hyperactivity.

2. *Central Nervous System.*—In a number of cases, morphologic changes in the central nervous system have been observed, particularly in the hypothalamic centers; furthermore, hemorrhagic foci were found in the region of the vagal nucleus. In such cases, the entire brain shows marked changes reminding the pathologist of encephalitis.

There is a neurogenic conception of the etiology of the disease (Sunder-Plassmann[54]). A neurologic connection to the thyroid has been established by the discovery in the thyroid of a neurohormonal cellular system connected through the parasympathetic system with the vascular endothelium and the thyrocytes of the follicles. These neurohormonal cells are distributed throughout the parasympathetic system and the endocrine glands; they form an independent parenchyma within the thyroid, and they determine the normal and abnormal output of the thyroid. The significant factor in exophthalmic goiter is the unrestrained absorption of both the stored and newly secreted colloid material.

Crises occurring spontaneously during conservative treatment show an extreme upset of the sympathetic nervous system and are caused by the unrestricted absorption by the neurohormonal cells and in the immediate postoperative period by thyroidectomy.

There is abundant clinical evidence (Marañon,[37] Étienne and Richard,[18] Merklen,[40] Railliet,[47] Kahane,[27] Rothackers,[48] Johnson,[26] Bär,[2] and Dannehl,[15]) that an enormous number of cases of Graves' syndrome arose as the result of fear during World War I. Crile[13] expressed the opinion that the characteristic facies and most of the symptoms of the patient with Graves' syndrome and those in man or in an animal in a state of fear are remarkably alike. As long ago as 1899, Darwin and Sir Charles Bell noted the marked neurogenic manifestations in toxic

patients of any sudden stimulation such as grief or anger, or other violent excitatory cause.

> The heart beats quickly and violently so that it palpitates or knocks against the ribs; there is trembling of all the muscles of the body; the eyes start forward and the uncovered and protruding eyeballs are fixed on the subject of terror; the skin breaks into a cold and clammy sweat, and the face and neck are flushed or pallid; the intestines are affected.

The phenomena of fear as thus indicated has many resemblances to the phenomena of an epileptic attack and convulsion. The close relationship of epilepsy and exophthalmic goiter was seen and commented upon by Patman.[43] Other observers remarked that each of these conditions had the same specific symptoms.

Apparently the nervous component of thyrotoxicosis is unrelieved by treatment (medical, thyroidectomy, etc.), possibly because the nervous pathways have become too firmly established and too responsive. In some cases these residuals represent a true psychoneurosis. The differentiation between toxic residuals and psychoneurosis is of prognostic significance. Follow-up studies show that there is a comparatively heavy incidence of nervous disorders after thyroidectomy, which would indicate that the operation removes only the most important glandular component and leaves the fundamental disorder untouched.

Diaz and Lorente[16] observed that the patients with exophthalmic goiter and with migraine eliminated during their crisis a substance with an intense acetylcholine effect, and they direct attention to the role of acetylcholine in the excitation of the sympathetic nervous system.

DISCUSSION

If one analyzes this factual knowledge, one is impressed by the following groups of clinical manifestations:

1. The frequent familiar constitutional tendency (Charcot,[11] Sattler,[50] Bauer,[5] Ostwald,[42] Pässler,[45] Holst,[25] Barker,[3] Falta,[19] Biedl,[6] and Buschan[10]). Most clinicians have noted its occasional occurrence in two or more members of the same family (Sattler,[50] Buschan,[10] Lerrede and Drouet,[33] Moss,[41] Bauer,[5] Chvostek,[12] Falta,[19] and numerous others). Less frequently, Graves' disease has been reported as occurring in mother and child (Sattler,[50] Bauer,[5] Lenz[32]).

A case is described in which a hysterical woman had ten children, eight of whom had exophthalmic goiter. One of the children had four grandchildren, three of whom had exophthalmic goiter and one of these was also hysterical.[49]

Souques and Lermoyez[53] saw sixteen such instances in adult members of one family during the course of three generations.

2. The onset of the illness is commonly referred to some well-defined incident or episode which is so recognizable to the patient that he very often voluntarily gives this information. In the exceptions, it is highly

probable that some such incident did occur, but, for some reason, most probably its insignificant or insidious character, it was not registered in the patient's mind.

The fact that the disease might originate very acutely and progress with great rapidity only emphasizes this point all the more. The characteristics of the nonoperative crises are very similar to the original manifestations at the time of onset of the total illness. In the postoperative cases, the evidence is overwhelming and is universally accepted, that the crisis is precipitated by the operation on the thyroid. The fact that crises may be originated after other types of operation, or after the many trivial and important causes previously referred to in this communication, indicates that in every case there has occurred a definite event which has preceded the crisis.

The fact that in the nonoperative crises there are examples in which no definite cause can be demonstrated does not alter the preceding statement necessarily. It means, perhaps, that the cause has been too trivial to register, as a single incident, but that it has been repeated many times; that in the discomforts of the illness, the patient did not appreciate or perceive the provocative cause; or that the powers of observation of the physician have not been sufficient to expose these causes, or that he was not available when they occurred.

3. In recurrent or persistent thyrotoxicosis, both in medically and surgically treated patients, the same factors and causes, including physical and psychic trauma, pregnancy, infections, etc., are always responsible for the exacerbation, recurrence, or persistence of the toxic state. The acuteness and severity of these manifestations vary as in the original stage of the disease and are of similar pattern. It is important to remember that this type occurs without, as well as after, operation.

4. No method of treatment, medical or surgical, actually "cures" the patient. No evidence exists that iodine, x-ray, or operation is curative, as the physician would know if he followed his supposedly cured patients until the end of their lives. Iodine brings about remissions of toxicity. It prevents aggravated manifestations of toxicity over long periods of time. It mitigates the severity of exacerbations which occur in the natural course of the disease. Anatomically, it produces involutionary changes in the gland. But by the same token, no gland is ever brought back by iodine to an entirely normal state, and clinically no toxic patient can ever be permanently cured by it. The stimulus to disease remains; sooner or later the gland returns to activity, and the toxicity flares up anew, as soon as iodine is withheld.

Anatomically, the following changes occur:

The first stage is that of hyperplasis, well recognized by the accompanying general symptomatology, including the thrill and bruit over the thyroid area. It is the stage of toxicity of hypervascularization.

The second stage is that of the so-called "resting" thyroid in which there is a tremendous accumulation of colloid within the acini. Con-

comitantly, the metabolic rate drops markedly toward or into the normal or minus rating, the weight increases, and there is a reduction of the heart rate to a satisfactory figure. But the exophthalmos may be unaltered or only slightly improved and in a certain percentage of instances (marked by a tendency toward excess weight) a little more prominent.

In the third stage thyroid involution occurs and in some cases atrophy actually occurs.

After operation, it appears as if the course and development of the disease has been cut off and stopped at the stage and time of the performance of the operation. The basal metabolism decreases more rapidly when subtotal thyroidectomy is performed than after medical treatment, because the thyroid gland is responsible for 40 per cent of the body heat (Dubois[17]). The patient gains weight, the pulse rate drops, and the tremor subsides to a degree. But, nevertheless, in spite of the fact that the patient states that he is "well," physical examinaion of the patient discloses that all of the previously existing objective symptoms and elicitable signs and manifestations are still present, including among others, the cardinal symptoms of thyrotoxicosis or exophthalmic goiter—nervousness or elicitable nervous symptoms and manifestations, rapid pulse exophthalmos, etc.

5. The secondary manifestations (complications of thyrotoxic disease including congestive heart failure, nitrogen retention, vomiting, diarrhea, rapid weight loss, emotional instability, an abnormally low index of respiratory stability (Bartlett[4]), an abnormally low liver function (Quick[46]), and an unsatisfactory exercise test (Bartlett[4]) are only temporarily, incompletely and sometimes not at all relieved, and are constantly subject to recurrences and exacerbations, so that the patient must be under constant medical surveillance.

In post-mortem room experiences, one is confronted with the following findings:

The Thymus.—In many cases a large thymus is found. It was found in from about 80 to 90 per cent of the fatal cases of Graves' disease by Seelig;[52] and Haberer[57] found a large thymus in 100 per cent of those patients dying from operation. Kocher[29] found an enlarged thymus in about 50 per cent and Hammer[23] in about 63 per cent of all patients with Graves' syndrome.

The first report of the association of a hypertrophied thymus with thyroid disease was made by Markham[38] in 1858. Numerous reports confirming his observations are in the literature (Matti,[39] MacKenzie,[34] Blackford and Freligh,[7] Crotti,[14] Giordano,[21] Potter,[58] and Margolis[36]). Blackford and Freligh,[7] in a study of 117 necropsies on patients who had had thyroid disease, found hypertrophy of the thymus in every patient under 40 years of age with a hyperplastic gland and in every patient under 30 years of age with a nonhyperplastic gland. They considered thymic hypertrophy and lymphoid hyperplasia a result rather than a contributing factor to the thyrotoxicosis. Margolis,[36] in a more

recent post-mortem study of eighty-five cases of thyroid disease, observed hyperplasia of the thymus gland in 85 per cent of the patients with exophthalmic goiter and in 53 per cent of the patients with adenomatous goiter. He thought that the possible significance of the hyperplasia may represent a constitutional, inherent disposition to the development of hyperthyroidism.

The rapid development of the thyroid crisis and the frequent, often sudden, death of the patient have led to the belief that the complication may be associated in some way with a dysfunction of the thymus. Thymic death, however, does not resemble in many respects death from thyroid crisis, but the majority of patients dying in crisis are found, at autopsy, to have a persistent and hypertrophied thymus.

The muscular weakness manifesting itself in patients with Basedow's disease as well as the adynamia, which, in coma, finally develops into myasthenia, is regarded as the effect of the thyroid hormone upon the chemical metabolism of the musculature. In numerous casuistic observations, the coincidence of thymic enlargement and myasthenic symptoms has been noted.

That Graves' syndrome and thymic enlargement are not simultaneous reactions to the same insult is shown by the frequency with which they are totally dissociated in the same patient. It is well known that persons with the thymic constitution are extraordinarily sensitive, not only to physical influences such as traumatism, narcosis, infections, etc., but also to psychic influences. The latter is proved by the frequency of suicides and of neuroses among such patients (Koliski,[30] and Paratascheww[44]). As the essential characteristic of the constitution of Graves' syndrome is the extraordinary sensitivity to physical and psychic stimuli, is it not reasonable to assume that the thymic constitution is merely a potential basis, not necessarily universal, for the development of Graves' syndrome?

The Liver.—In the cases reported by Foss, Hunt, and McMillan,[20] there was only one normal liver in the patients dying during true crisis. Ten of the eleven subjects showed varying degrees of necrosis in the center of the lobules. There were eight necropsies in which fatty degeneration of the liver cells was a prominent feature. This change was more marked in the livers in which necrosis was extensive. Cellular infiltration was present in three organs and congestion in one, the latter occurring in a patient who had healed mitral endocarditis.

The liver changes are remarkable. In the liver the action apparently starts at the periphery of the lobule and produces a parenchymatous degeneration of the cells similar to that produced by other toxic agents. There is a marked reduction in fat and an almost complete absence of glycogen, factors which probably preceded the degenerative changes. The fibrosis probably indicates a preceding condition of hepatitis, that is, hyperemia, edema, and degeneration without lymphocytic or leucocytic reaction.

Two types of liver parenchymal cells are responsible for the varied hepatic functions. The reticuloendothelial Kupffer cells clear the hepatic blood of particulate matter and share in the formation of antibodies and antitoxins. Each hepatic cell is a unit in itself, contributing its share to the multifold functions attributed to the liver as an organ.

In order to produce experimental hyperthyroidism, Sciaky[51] used thyroxin by hypodermic injection. The anatomic findings resemble those seen in acute and chronic clinical cases which have come to autopsy. The findings consisted of loss of weight and visceral changes in the liver, heart, kidneys, spleen, hypophysis, parathyroids, and pancreas. In the heart and liver, they were characterized by a richly vascularized fibrosis. In clinical medicine, liver changes are found in all cases of thyrotoxicosis and form an important part of the total illness (see Discussion).

The pancreas of the guinea pigs presented remarkable modifications. In the acute intoxication, there was degeneration amounting almost to necrosis of the islets. In the chronic intoxication, there was hypertrophy of the insular apparatus amounting to two or three times that found in the normal. The application of these experimental facts may indicate that the thyroid hormone stimulates pancreatic hyperplasia, which in turn empties the liver of its reserves.

The incorporation of the function of antibody activity and the protection against disease in the many and various physiologic activities of the liver are well known. In cellular destruction of the liver parenchyma, all functions are lessened and deteriorated. In thyrotoxic disease, it is well known that the liver abnormality is a most important factor.

Maddock and his associates[55] conclude that (1) preoperative studies of the hepatic function give no indication of the mildness or severity of the postoperative course, and (2) in the postoperative period there is an increase in the impairment of the hepatic function, with an increase in hyperthyroid reactions, but no evidence to show that one is the cause of the other. Lesions in the liver appear to be an integral part of the syndrome of severe toxic goiter.

Comparison With Certain Factual Knowledge of Allergic Conditions.—Recent research has indicated that certain relatively obscure diseases may be dependent upon an increased reactivity of tissue to various known and obscure antigenic substances. Allergic responses occur in a large number of diverse conditions, can be demonstrated by skin reactions which are specific for some only, and are probably caused by some cellular protein substance or by other products of cellular metabolism. Frequently the reaction is a nonspecific one.

Weil[55] believes that anaphylactic and allergic reactions are of a cellular and not a humoral character, because he was unable to demonstrate the presence of any antigenic substance in the blood of experimental animals. He is convinced that the site of the reaction is in the paren-

chymal cells of the liver. In his experimental animals, Weil found that the liver dominates the entire picture: in the very severe cases, the organ is tremendously enlarged; it is intensely cyanotic and bleeds freely on section; the parenchymal cells show varying degrees of congestion and hemorrhage, clouding, swelling, and in severe cases, a disseminated necrosis.

In long-standing cases, the liver changes are even more marked and assume a chronic character even to certain fibrotic changes. Changes in the other organs are very similar to those described by Sciaky[51] (see Discussion).

Neurologic Allergy.—The association of asthma, urticaria, migraine, and epilepsy has long been known. According to Blanton[8] and to Kennedy,[28] the brain, meninges, and nerve trunks are all subject to the allergic reaction, characterized by vascular spasm and dilatation, sudden localized edema, and cellular infiltration (focal angioneurotic edema), and reflecting the location and degree of focal injury. According to Kennedy,[28] such focal areas (1) involving the brain substance cause epilepsy; (2) involving the meninges with painful stretching cause migraine; (3) involving nerve roots and trunks cause evanescent peripheral motor paralysis, and (4) that many cases of "transient palsies," retrobulbar neuritis, and maladies of peripheral nerves and spinal roots are all due to protein sensitization.

Changes in the brain during a migrainous attack were actually observed by Goltman[22] in a patient with a cerebral decompression. In the initial stage the patient's face was pale and the area of decompression sunken (vasomotor spasm). With the appearance of headache and vomiting the face became suffused and through the decompression opening a bulging mass appeared (vascular dilatation and edema).

SUMMARY AND CONCLUSIONS

One must accept Hertzler's[24] conception of all thyroid disease as one continuous disease process. One must then arrrive at the conclusion that some underlying condition is present, that the patients have been suffering from latent if not active toxicity for very long periods of time, and that all the manifestations, including all exacerbations and recurrences, are episodes of a single disease.

Very acute onsets, and all sudden exacerbations including all crises are due to the sudden release of some factor which acts in a very powerful manner, apparently through the thyroid, as an antigenic and/or catalytic agent in an already sensitized individual.

Thyroid operation in thyrotoxicosis followed by a thyroid crisis represents a laboratory experiment in which a successful "take" has occurred. The large number of "takes" only emphasizes this fact. The difficulty in understanding this sequence of events is due to the fact that the pathogenesis of this sequence is rarely made clear by post-mortem examination. In this state it is obvious that there are profound toxemia

and a violent and overwhelming disturbance of metabolic processes with, no doubt, a profoundly altered blood chemistry. Studies on the blood chemical variations in a state of crisis have not yielded satisfactory results, because the causal body has not yet been identified and cannot, therefore, be measured.

There is no doubt that the study and understanding of thyrotoxic crises furnishes the best approach and clue to the understanding of thyrotoxicosis in general.

Neurologic pathways and a neurohormonal cellular system have been demonstrated (Sunder-Plassmann[54]) whereby an excitatory cause could be quickly distributed and could bring about the acute and hyperacute onsets, and the equally acute exacerbations and crises. There is further factual knowledge regarding many similarities between thyrotoxicosis, neurologic allergy, epilepsy, and certain mental states, especially fear.

After the disease has been present for some time, the demonstrable pathologic-anatomic changes in thyrotoxicosis (Basedow's disease, exophthalmic goiter) are very similar to those seen in equally long-standing cases of allergic disease. In this regard the liver changes are especially important, and the knowledge of this anatomic and clinical association is well spread by this time. Because of inherent physiologic functions of the liver, this has special reference to sensitization and antibody formation.

This factual, clinical, and pathologic evidence seems overwhelmingly in favor of the viewpoint that thyrotoxicosis must be classified—at least as far as its pathogenetic mechanism is concerned—with the allergic group of diseases.

In the medical treatment of thyrotoxicosis and in the preparation of thyrotoxic patients for operation, iodine (Lugol's solution) seems to exert its beneficial effect by decreasing the sensitization of the patient. The occasional uncontrolled effect which it sometimes causes is in line with the occasional similar action of other antigenic bodies.

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COTTON SUTURES IN SURGERY OF WARFARE

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MEADE and Ochsner,[1] in 1939, suggested that cotton thread would be a very satisfactory suture for employment in war injuries in the field. One of the early reports of the use of cotton in present-day field surgery came from a 750 bed field hospital, shortly after the conclusion of the Carolina maneuvers of 1941, and embodied an analysis of 124 clean, contaminated, and infected wounds wherein cotton had been employed. The results obtained thereby were in support of the contention of Meade and Ochsner heretofore stated.

The current report describes further experiences with cotton sutures during a period of duty in the Southwest Pacific Area. In some situations the type of surgery performed has been analogous to that of the ordinary station hospital, while at other times it has consisted principally of the care of battle casualties. The work has been performed in a variety of circumstances—sometimes in modern buildings, sometimes in tents or makeshift shelters, and oftentimes in situations where some contamination by insects was unavoidable.

Throughout this time the employment of cotton for sutures and ligatures has been in the nature of a routine procedure, although there have been some fairly constant exceptions. Stainless steel wire has been regarded as the suture of choice for the actual repair of tendons, although cotton has been used for hemostasis and for closure in such cases. Catgut has been employed regularly in rectal surgery and for the mucosal suture in operations upon the gastrointestinal tract. Heavy braided silk is preferred for through-and-through closure of the abdomen. With occasional further exceptions cotton has been employed routinely.

Only nonmercerized cotton has been used. Interrupted suture technique has generally been employed. Quilting cotton (No. 50), either single or double, has been the size most frequently selected. When a finer suture was adequate, No. 70 or No. 100 was used. Ligation of large arteries was accomplished with No. 16 cotton.

COTTON SUTURES IN SURGERY OTHER THAN ON BATTLE CASUALTIES

The series for which cotton sutures were used in surgery other than on battle casualties consists of 534 major and minor operations of all types in which cotton was the sole or predominant suture. A detailed analysis of the cases constituting this series is given in Table I.

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TABLE I

Appendectomy		174
Hernia, inguinal		53
Hernia, umbilical or epigastric		11
Cholecystectomy		2
Perforated peptic ulcer		2
Gangrene of epiploic appendix		1
Rupture of liver		1
Appendical abscess		1
Cecostomy		1
Sigmoid colostomy		2
Retroperitoneal tumor		2
Resection or repair of perforation of bowel		2
Release of small bowel obstruction		2
Closure of fecal fistula		1
Suprapubic cystostomy		5
Subtemporal decompression		1
Cranial burr holes		2
Aneurysm of superficial temporal artery		1
Mixed tumor of parotid gland		2
Thyroid adenoma		3
Thyroglossal duct cyst		1
Branchial cleft cyst		2
Tracheotomy		1
Excision of male breast		8
Hydrocele		2
Excision of small benign tumors, cysts, etc.		55
Saphenous ligation		22
Plastic revision of cicatrix		16
Primary closure of fresh laceration		46
Repair of lacerated tendon		15
Débridement of soft tissue wound		13
Débridement of compound fracture		31
Skull	7	
Sacrum	1	
Humerus	2	
Radius and/or ulna	1	
Carpals, metacarpals, and phalanges	9	
Tibia and/or fibula	5	
Tarsals and metatarsals	6	
Amputation		10
Mid-thigh	1	
Midleg	1	
Digit	8	
Open reduction and internal fixation, simple fracture		12
Mandible	1	
Humerus	1	
Radius and ulna	1	
Femur	4	
Tibia and fibula	3	
Tarsals and metatarsals	1	
Patella	1	
Débridement of wound of joint without fracture		2
Osteoplasty		7
Excision of bursa		5
Removal of loose body from joint		6
Acromioclavicular separation		2
Excision of semilunar cartilage		9

In this series only four complications which bear any apparent relation to the type of suture material are known to have occurred. In each of three hernias, repair was followed by a persistent draining sinus for correction of which a subsequent operation was performed. In one case of peritonitis, evisceration occurred following layer closure of the abdomen with cotton sutures.

In enumerating these complications, due cognizance must be taken of the fact that our opportunities for prolonged clinical follow-up are infrequent and that other complications may have arisen of which we have no knowledge. That their incidence should be large, however, is unlikely, inasmuch as patients were ordinarily retained in the hospital until they were able to resume full duty status. We have seen occasional instances in which, some months after operation, a subcutaneous ligature could be palpated through the operative scar, in spite of the fact that only the finest sizes of cotton were used in such locations.

In addition to the series just presented, cotton has been used as a routine hemostatic ligature in minor contaminated operations such as incision and drainage of abscesses or excision of pilonidal sinuses. No hindrance to wound healing which could be attributed to cotton was observed.

COTTON SUTURES IN THE SURGERY OF BATTLE CASUALTIES

The war wounds comprising the series in which cotton sutures were used in the surgery of battle casualties are 237 in number. The average interval between injury and arrival at this hospital was three to four days. The majority of patients in this group underwent their initial major surgery at our hands, the notable exceptions being in wounds of the abdomen and chest. Gross contamination of wounds was the rule, and infection had often become established to the point of frank suppuration. Meade and Ochsner[3] have expressed the belief that the most important use of nonabsorbable suture material is in grossly contaminated cases.

The usual operative procedure consisted of the following: Careful cleansing of the skin; saucerization of the wound or unroofing of long tunnels; excision of all devitalized tissue; relaxation of incisions of enveloping fascias; removal of fragments of bone, metal, blood clots, or other debris; irrigation with normal saline solution; introduction of a thin film of sulfanilamide; loose application of petrolatum gauze, followed, when possible, by incorporation in padded plaster casts. Cotton ligatures were employed routinely in these cases. We were fortunate in having been so situated that the patients remained under our care for periods sufficiently long to permit adequate observations of the nature of healing in most wounds.

A detailed analysis of the cases constituting this series is given in Table II.

It is of interest to add that in forty-five instances Thiersch grafts were subsequently performed upon wounds in this series. It was the invariable rule that healthy granulation tissue grew over and covered such cotton as was implanted in the wounds, with resultant smooth granulating surfaces which were altogether satisfactory for the application of grafts.

TABLE II

Sigmoid colostomy		3
Release of small bowel obstruction		1
Subphrenic abscess		1
Perinephritic abscess		2
Intra-abdominal abscess		2
Suprapubic cystostomy		1
Traumatic arterial aneurysm		3
Axillary	1	
Brachial	1	
Radial	1	
Débridement of wound involving soft tissue only		111
Scalp and face	4	
Thorax	19	
Buttocks and sacrum	8	
Penis, scrotum, and perineum	6	
Arm	12	
Forearm	9	
Hand and fingers	6	
Thigh	27	
Leg	17	
Foot	3	
Débridement of compound fracture		86
Skull	7	
Facial bones (including mandible)	6	
Clavicle	1	
Scapula	2	
Humerus	9	
Radius and/or ulna	9	
Carpals, metacarpals, and phalanges	7	
Ribs	9	
Pelvic bones	3	
Femur	8	
Tibia and/or fibula	8	
Patella	5	
Tarsals, metatarsals, and phalanges	12	
Amputation		16
Arm	3	
Thigh	4	
Tarsometatarsal	1	
Carpal	2	
Digits	6	
Débridement of wound of joint without fracture		4
Open reduction and internal fixation of simple fracture		3
Radius and ulna	1	
Humerus	1	
Femur	1	
Débridement and drainage of osteomyelitis	4	
Ulna	1	
Clavicle	1	
Ileum	1	
Femur	1	

No untoward effect could be attributed either directly or indirectly to the use of cotton in any one of the 237 cases constituting this series.

SUMMARY

Cotton has been adopted as the preferred suture material for surgical use at a 750 bed hospital in the Southwest Pacific Area. With occasional exceptions it has been used routinely. The series reported upon comprises 534 major and minor operations other than upon battle casualties

and 237 operations upon battle casualties. The latter group in particular includes many cases in which the wounds were extensively contaminated or grossly infected at the time of initial operation.

CONCLUSION

Cotton suture material may be employed safely and with highly satisfactory results in the surgery of war wounds without regard either to their degree of contamination and infection or to the elapse of time between injury and the institution of definitive surgery.

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THE SURGICAL AND ANATOMIC SIGNIFICANCE OF THE MAMMILLARY TUBERCLE OF THE LAST THORACIC VERTEBRA

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IN THE course of observations made on the mounted skeletons in the laboratory of the department of anatomy of the College of Physicians and Surgeons at Columbia University, I noticed that the mammillary process of the twelfth thoracic vertebra greatly differs from that of all other vertebrae in its shape and relationship to the superior articular process. It was thought that the specific character of the mammillary process of the twelfth thoracic vertebra could be responsible for a comparative inaccessibility to the articulation between the eleventh and twelfth vertebral articular processes and, thus, account for the nonunion in this area, as observed occasionally after spine fusion operations by the method of Hibbs.

In reviewing the extensive literature on this subject, it was found that one of the difficulties encountered was the nomenclature of the smaller processes of the vertebra, when attempts are made by the authors to define homologous structures. It is necessary, therefore, to correlate the nomenclature used by other authors with the nomenclature used in this article.

The twelfth dorsal vertebra represents the last thoracic vertebra in the human spine. In other mammals the number of dorsal vertebrae varies greatly. It is usually more than twelve. In the anthropoid apes the usual number is thirteen.

THE MAMMILLARY TUBERCLE

The human twelfth dorsal vertebra consists of a body which is connected by two short pedicles with the superior and inferior articular processes situated posteriorly; two short transverse processes are placed laterally and behind the superior articular processes. The transverse processes of this vertebra differ greatly from the corresponding ones of the other vertebrae. They are shorter than the others and appear rudimentary. They show variations which are either symmetrical or asymmetrical. These variations may be comparable to the variations of the articular processes observed by Whitney, who found that the asymmetry of articular processes is of relatively frequent occurrence and is limited to the last two rib-bearing vertebrae, and that there might be a relation between these variations and exaggerated handedness associated with certain professions.

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The transverse process of the twelfth dorsal vertebra presents three tubercles or smaller processes: the superior, the lateral, and the inferior or accessory. The corresponding nomenclature and homologies of the tubercles, as accepted by a number of anatomists, are shown in Table I.

TABLE I

COMPARATIVE TERMINOLOGY OF THE TRANSVERSE AND RELATED PROCESSES OF THE ELEVENTH AND TWELFTH DORSAL AND FIRST LUMBAR VERTEBRAE

ELEVENTH DORSAL	TWELFTH DORSAL	FIRST LUMBAR	
Transverse process	(1) Mammillary tubercle or superior process	(1) Mammillary tubercle or superior process	(1) Mammillary tubercle, Owen's metapophysis
	(2) Lateral process	(2) Lateral process	(2) Homolog. of transverse process of dorsal vertebra
	Transverse process	Transverse process	
	(3) Inferior process	(3) Inferior process	(3) Accessory process or Owen's anapophysis
Rib	Rib		(4) Costal process

In the course of examination of specimens of human spines, it was noticed repeatedly that the mammillary or superior process of the twelfth dorsal vertebra is much longer and stouter than the corresponding process of the eleventh dorsal or first lumbar vertebra. It was also noticed that the mammillary process is absent on all dorsal vertebrae above the eleventh. An important relation was found between the mammillary process and the superior articular process. This relation was not found in the lumbar vertebrae and seemed to be confined to the twelfth dorsal vertebra only, although sometimes the eleventh dorsal showed a similar but very much less pronounced disposition. When the twelfth dorsal vertebra is examined from the side, the mammillary process is found behind the superior articular process with a deep depression separating the two processes. When observed from its posterior aspect, the mammillary process seems to conceal the superior articular process. A comparison with the eleventh dorsal vertebra shows that the mammillary process is considerably smaller and is placed farther back from the superior articular process. The first lumbar vertebra has a completely different relationship; the superior articular process and the mammillary process are in the same plane, the articular process seems to be in direct continuation with the mammillary process, and there is no intervening depression between them (Figs. 1*A*, 1*B*, and 1*C*). Figs. 2 and 3 represent lateral and posterior photographs of the twelfth dorsal vertebra.

The depression between the superior articular process and the mammillary process of the twelfth vertebra (Fig. 3) forms an angle which in this illustration equals about 67 degrees. The relation of the length of the superior articular process from the apex of the depression to the length of the mammillary tubercle from the apex of the depression is 28:23. The relation of the actual height of the superior articular process to the height of the mammillary tubercle is 25:27. This method

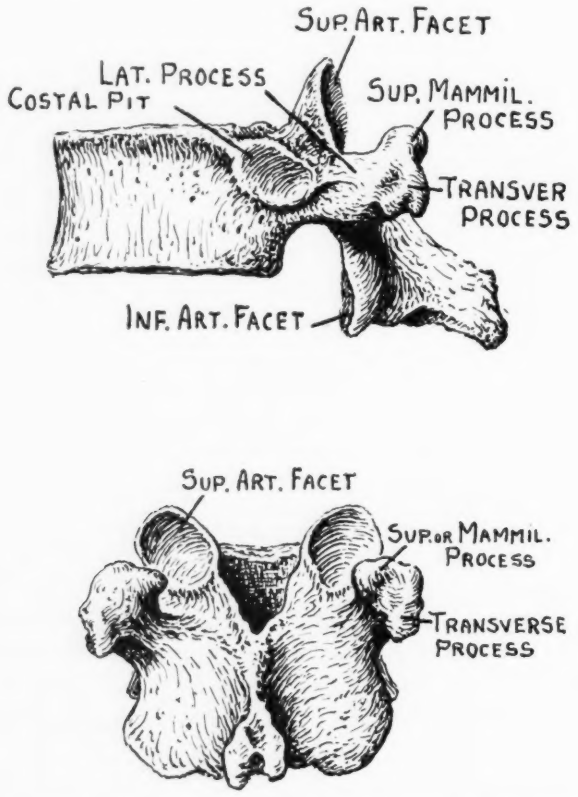


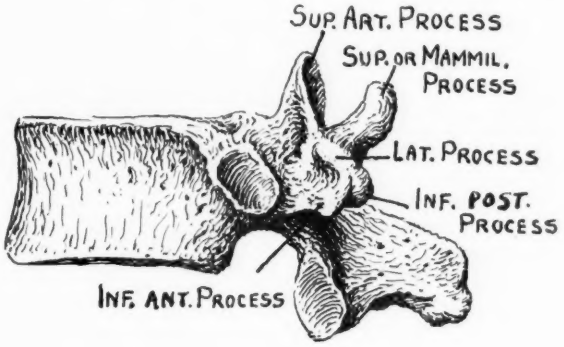
Fig. 1A.—The human eleventh dorsal vertebra for comparison with Fig. 1*B* and Fig 1*C*.

of measurement, represented in Fig. 4, was applied to an analysis of the last two dorsal and first lumbar vertebrae in a series of white and Negro, male and female patients. The results of the measurement showed that the height of the mammillary process of the twelfth dorsal varied in relation to the height of the superior articular process but was almost invariably much higher than the mammillary process of the eleventh.

The angle between the superior articular and mammillary processes varied from 50 to 90 degrees. With the increase of the angle, the articular facet was found to be inclined more forward so that the cartilaginous surface of the facet was found to be directed more cephalad. The angles on the left and right sides were not always

symmetrical. In 43 per cent of the spines examined, the angle on the right side was greater. In 36 per cent it was found greater on the left side, and only in 21 per cent was it found symmetrical. The difference between the angles varied from 5 to 10 degrees and in one case reached 28 degrees. No great significance was attached to this variability. It may have the same significance as the variation of the articular processes as observed by Whitney and mentioned previously.

It is shown in Table II that although the mammillary tubercle of the eleventh vertebra may reach in certain instances less than one-half of the height of the superior articular process, in the majority of the examined spines, the height of the mammillary process of this vertebra



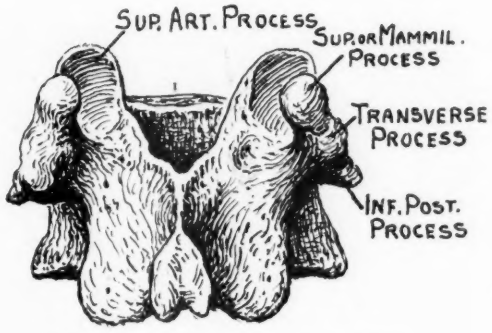


Fig. 1*B*.—Twelfth dorsal vertebra.

was almost insignificant in comparison with the height of the mammillary process of the twelfth vertebra. In one case the mammillary processes of the twelfth vertebra were of the type encountered on the eleventh vertebra, but in this case there was apparently an additional dorsal vertebra, because the first lumbar had all the characteristics of a dorsal vertebra. The mammillary process of the twelfth vertebra, in more than one-half of the examined spines, equaled more than one-half, or about one-half the height of the superior articular process.

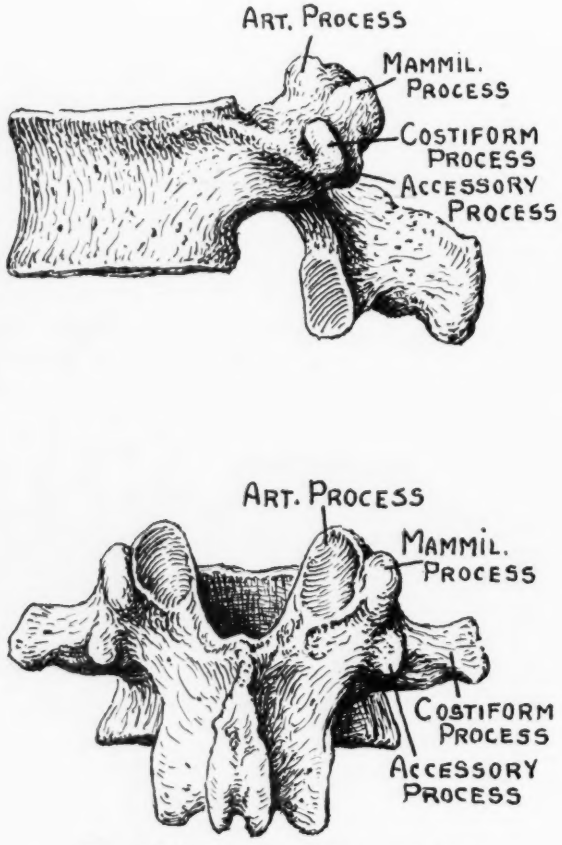


Fig. 1*C*.—The first lumbar vertebra.

Fig. 2.—Photograph of the posterior view of the twelfth human vertebra.

There was no visible mammillary process on the tenth dorsal vertebra and none above the tenth. The mammillary process of the lumbar vertebra, as mentioned before, lies lateral to the articular process and does not resemble in the least the typical relation between the two processes. The specific relation of the tubercle seen on the isolated twelfth vertebra was found more interesting on the mounted skeleton

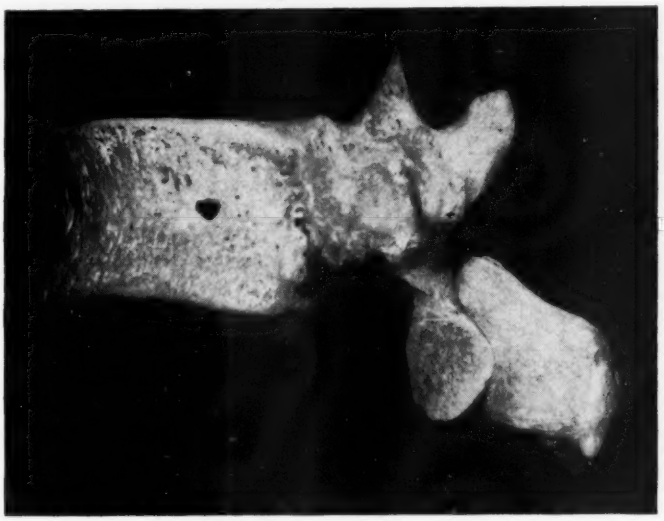


Fig. 3.—Photograph of the lateral view of the twelfth human vertebra.

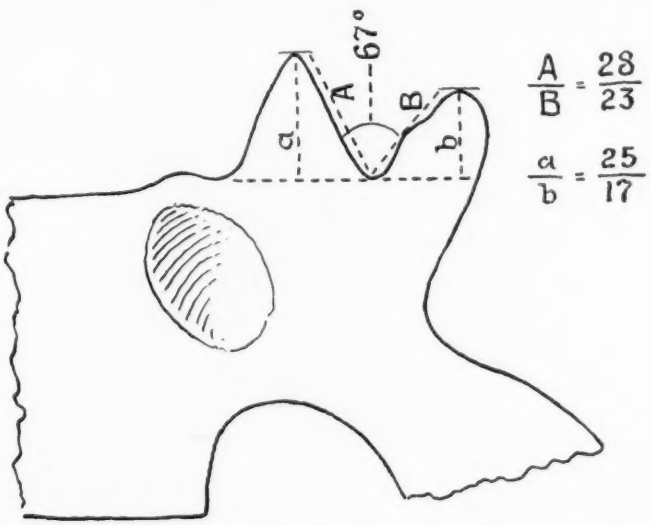


Fig. 4.—Method of measurement of the ratio between the height of the mammillary and superior articular process.

(Fig. 5). Here the mammillary process of the twelfth vertebra covered the joint between the inferior articular process of the eleventh vertebra with the superior articular process of the twelfth from behind, so that the joint itself was somewhat concealed. The joint between the inferior articular process and the superior articular process

between the ninth and tenth and the tenth and eleventh dorsal vertebrae, as well as that between the twelfth dorsal and first lumbar, can be seen very well from behind because it is not obstructed by the large mammillary tubercle, as seen almost constantly on the twelfth dorsal vertebra.

Fig. 5.—Photograph of the right side of a mounted skeleton. The articulation at the top of the illustration is between the tenth and ninth dorsal vertebra. The lowest articulation is between the twelfth dorsal and first lumbar.

The relation of the tubercle to the articular process on the mounted skeleton induced an x-ray study of the area on living subjects. A review of over one hundred x-ray pictures of the spine disclosed that the relationship of the mammillary processes of the vertebrae was not visualized in the ordinary film. If need be, a special technique will probably have to be devised for visualization of the mammillary tubercles.

TABLE II

RATIO OF ACTUAL HEIGHT OF THE MAMMILLARY PROCESS TO THE ACTUAL HEIGHT OF THE SUPERIOR ARTICULAR PROCESS OF THE VERTEBRAE

NO.	ELEVENTH DORSAL		TWELFTH DORSAL		FIRST LUMBAR		REMARKS
	LEFT	RIGHT	LEFT	RIGHT	LEFT	RIGHT	
1	.33	.40	.66	.90			
2	.50	.07	.83	.83			
3	.23	.45	.50	.62			
4	.10	.10	.45	.30			
5	.08	.07	.30	.10	.90	.62	The lumbar is a typical last thoracic
6	.07	.06	.36	.45			
7	.30	.20	.50	.33			
8	.01	.01	.30	.25			
9	.01	.09	.50	.50			
10	.20	.18	.33	.17			There is a deep depression between the processes on the twelfth
11	.20	.40	.50	.50			
12	.17	.33	.60	.50			
13	.17	.15	.55	.50			
14	.07	.14	.43	Lumbar type			
15	.01	.01	.70	.25			
16	.30	.20	.23	.65			
17	.01	.01	.50	.60			
18	.02	.02	.40	.43			
19	.02	.03	.48	.45			
20	.03	.04	.46	.44			
21	.06	.08	.60	.50			

It may be of interest to note that the mammillary processes of the last thoracic, lumbar, and sacral vertebrae have special epiphyses which appear about the time of puberty and join the rest of the vertebrae after the eighteenth year.

COMPARATIVE ANATOMY

A systematic and detailed study of the comparative anatomy of the vertebral column belonging to different animal groups is a very large subject presenting obvious difficulties. It is not within the scope of this article. This study was restricted to observations on a limited available material. Useful information was obtained from examination of casual specimens of quadrupeds and anthropoid apes, on exhibition specimens in the American Museum of Natural History and also from the literature. I was also able to examine the spines of twenty gibbons of an excellent collection belonging to Dr. S. Washburn of the department of anatomy of the College of Physicians and Surgeons.

As a result of this study it was found that the mammillary process exists in a number of animals. It may assume a variety of forms and occupy a variable position in relation to the articular process and lamina. Vallois made valuable observations on the spine of Cetacea. He noticed that the mammillary process, found in the cervical and anterior dorsal spine, is located on the base of the transverse process, behind the articular process. Further in the posterior dorsal region the mammillary process migrates along the vertebral laminae toward the spinous process and becomes a feature of the spinous process on the vertebrae of the lumbar region. It then loses all relation to the articular process. In most of the amphibians it is usually extremely small and

does not bear any direct relation to the articular processes. Flower and Gadow described a peculiar relationship of the superior articular process and the mammillary process in the great anteater (Myrmecophaga jubata). This animal has a double superior articular process in the lower dorsal region. Close observation shows a small mammillary process situated somewhat above and entirely laterally on the eleventh dorsal vertebra. There is also a very small mammillary process in the lumbar region of this animal. The mammillary processes are described in domestic animals. In the horse, with eighteen thoracic vertebrae, a mammillary process is described in the last four or five vertebrae. The processes are located laterally to the anterior articular process of the vertebra. In the cow, with thirteen dorsal vertebrae, the mammillary process is found to be quite small and rounded and located laterally to the anteroir articular process. In the pig, with fourteen or fifteen dorsal vertebrae, a mammillary process is observed projecting laterally from the anterior articular process. In the dog, with thirteen dorsal vertebrae, the mammillary processes are observed on the last seven or eight dorsal vertebrae. They also project laterally to the anterior articular surface and are usually small.

Examination of three spines of gorillas, six of chimpanzees, and three of orangutans showed the presence of small mammillary processes on the last two thoracic and on the lumbar vertebrae. The mammillary processes of the dorsal vertebrae of the apes were very small and were situated laterally in relation to the articular superior process. The articulation between the eleventh and twelfth dorsal vertebrae was not covered by the mammillary process from behind as observed in the human spine. In general, in none of the examined animals did the mammillary process bear the same relation to the superior articular process of the twelfth vertebra as described in the human spine.

In the gibbon the mammillary process of the last two thoracic vertebrae showed a relationship to the superior articular process similar to that in the human being. The gibbon, as a rule, has thirteen dorsal vertebrae. The mammillary process of the last thoracic vertebra is located behind the superior articular process; there is a deep depression between the two processes and the joint between the twelfth inferior articular process and the thirteenth superior articular process is concealed by the mammillary process of the thirteenth thoracic vertebra in a manner similar to that found in the human being (Fig. 6). There is a great variability of the size of the mammillary process and a frequent transition of the larger mammillary process from the thirteenth to the one above or to the one below. Of the twenty gibbon spines examined, twelve showed the mammillary process on the thirteenth dorsal vertebra (last thoracic), six showed a shift to the twelfth dorsal (corresponding to the eleventh dorsal human vertebra), and two showed a typical lumbar structure.

Apparently the gibbon is the only animal with mammillary processes bearing a relationship to the superior or articular process similar to man. This fact may be of some importance since it is known that of all the mammals besides man, the gibbon is the only one which frequently assumes an orthograde biped position while running on the ground.

From the foregoing description it becomes apparent that: (1) the mammillary process is found universally in animals, (2) its position and size are variable in relation to the articular process, and (3) the existence of a large mammillary process of the twelfth human vertebra is similarly found only on the thirteenth (last thoracic) vertebra of the gibbon.

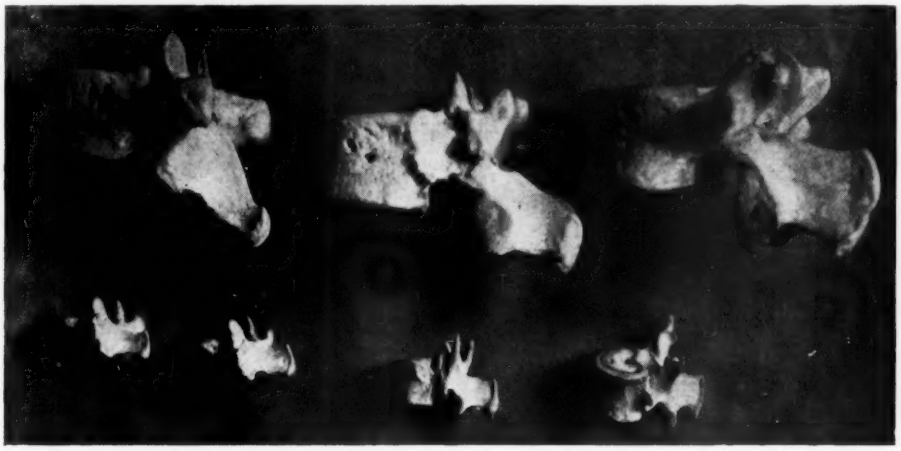


Fig. 6.—Comparative view of the eleventh and twelfth dorsal vertebra and first lumbar of a human specimen in the upper row. The eleventh, twelfth, and thirteenth dorsal and first lumbar of a gibbon specimen are shown in the lower row of this illustration.

The variability of the size and location of the mammillary process was investigated by Vallois, who established with a great degree of probability that in comparative anatomy the mammillary process is a migrating structure, occupying various places on the transverse process and laminae of the dorsal and lumbar vertebrae, according to functional demands and relative development of the transversospinal and longitudinal systems of the intrinsic dorsal muscles. The similarity of the mammillary process in man and the gibbon may suggest an interdependence between the two factors, mammillary process and orthograde biped position.

INTRINSIC MUSCLES OF THE SPINE

There are two groups of muscles which are of interest to us in the lower dorsal and upper lumbar region: the longitudinal consisting of a superficial and a deep layer, and the transversospinal consisting of three

layers. The longitudinal superficial system has three groups of muscles situated from the medial line outward in the following order: the spinalis dorsi, longissimus dorsi, and iliocostalis dorsi; the deep longitudinal group consists of the levatores costae in the dorsal region and of the intertransversarii system in the lumbar and dorsal region. The transversospinal group has three layers of which the most superficial is the semispinalis dorsi, the intermediate is represented by the multifidus, and the deep by the rotatores. It is important to review in brief the origin and insertions of all these muscles for further understanding of the significance of the mammillary process.

The Longitudinal Group.—The spinalis dorsi originates from the tips of the spinous processes of the first and second lumbar and twelfth and eleventh dorsal, and is inserted into the tips of the spinous processes of the first ten dorsal vertebrae. The longissimus dorsi has a common origin with the iliocostalis lumborum. About the level of the twelfth rib the separation of the two muscles becomes evident. The longissimus dorsi is inserted into the lower border, back of the accessory tubercles of the lumbar vertebrae, the lateral aspect of the mammillary process, and the inferior margin of the transverse processes of the thoracic vertebrae and the inferior margins of the ribs lateral to the costal tubercles. The iliocastalis dorsi coming up from the common mass takes additional origin from the superior border of the lower seven ribs, medial to the angles, and is inserted into the upper seven ribs near their angles and to the transverse process of the seventh cervical vertebra.

The Transversospinal Group.—The transversospinal muscles, difficult to dissect, and presenting multiple variations, are differently described by many authors. It seems that for clarity and simplicity, Trolard's description, as given by Testut, is perhaps the best. The semispinalis dorsi, the multifidus, and the rotatores all take origin from the medial side of the mammillary process and the corresponding upper border of the transverse processes according to the region involved. From this area of origin they divide into four different groups: (1) the spinous, directed toward the spinous process of the fourth vertebra above and corresponding to the semispinalis, (2) the subspinous, directed to the base of the spinous process of the third vertebra above and corresponding to the multifidus, (3) the long laminary, directed and inserted into the inferior border of the lamina of the second vertebra above and correresponding to the rotator longus, and (4) the short laminary, directed and inserted into the external aspect of the lamina of the first vertebra above and corresponding to the rotator brevis (see Fig. 7).

FUNCTIONAL SIGNIFICANCE OF THE MAMMILLARY PROCESS

A functional analysis of the spinal musculature in relation to motion of the trunk is a problem presenting many difficulties. When the area

under consideration is examined, two important factors stand out. The first is the generally accepted view that the line of gravity in the static orthograde position of the human spine passes through the body of the ninth dorsal vertebra or in its vicinity. The second factor is that the area of transition between the thoracic and lumbar vertebrae is associated with a functional transition of motion of the thoracic and lumbar spines. The thoracic spine is concerned mostly with torsion and lateral inclination, the lumbar spine with anteroposterior motion. The semispinalis and the multifidus, which originate from

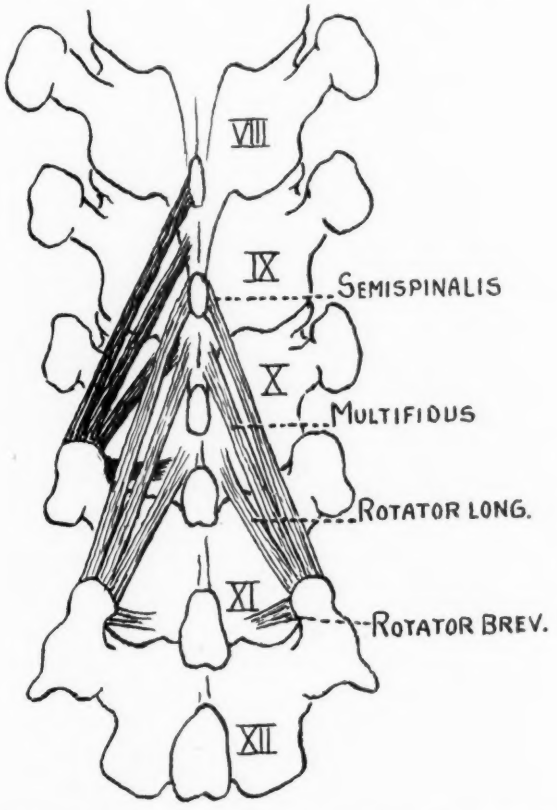


Fig. 7.—Schematic drawing of the intrinsic transversospinal muscles of the human dorsal spinal musculature after the description of Trolard.

the mammillary process of the twelfth vertebra, are inserted into the spinous process of the ninth and into the base of the tenth. Together with the rotator muscles they form a strong group which probably plays an important role in this area of functional transition. The size of the mammillary process of the twelfth vertebra is probably related to the functional demand upon the muscles originating from it.

THE SURGICAL SIGNIFICANCE OF THE MAMMILLARY PROCESS

The presence of a prominent mammillary process on the twelfth dorsal vertebra is important for two reasons. It may serve as a useful

landmark in the posterior surgical approach to the spine. When the spinous processes of the lower dorsal and upper lumbar vertebrae are exposed and further exposure of the laminae is obtained, it will be noticed, proceeding from the dorsal to the lumbar vertebrae, that the space between the spinous processes in the midline and the transverse processes laterally becomes narrower. Palpation of the lateral side of this space will reveal to the palpating finger a slight prominence corresponding to the mammillary process of the eleventh vertebra. Just

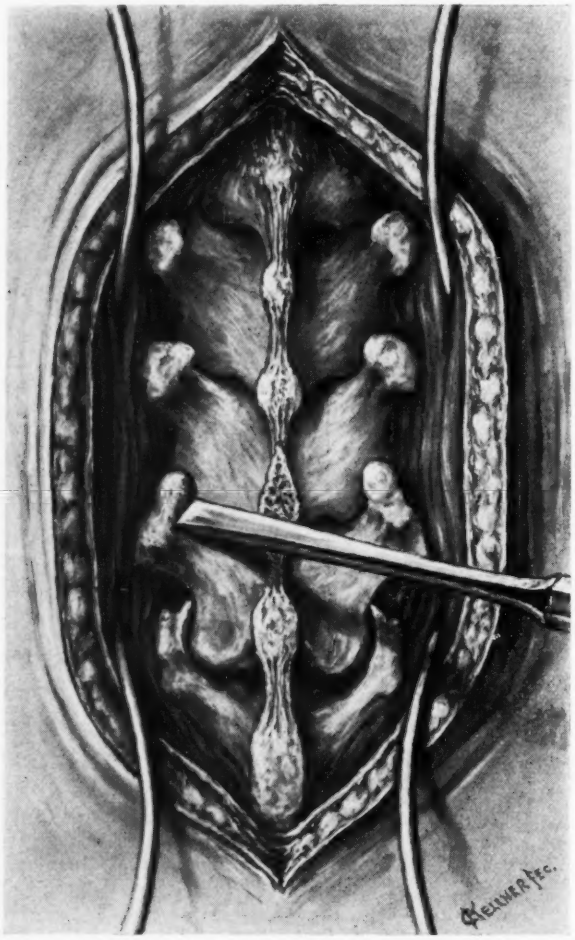


Fig. 8.—Surgical exposure of the lower dorsal vertebra with resection of the mammillary process of the twelfth dorsal vertebra.

below this a much larger prominence will be felt and this will correspond to the mammillary process of the twelfth vertebra, which in its turn will indicate the position of this vertebra.

Fig. 5 indicates clearly the second reason for the importance of the mammillary process. It conceals the articulation between the inferior articular facet of the eleventh and the superior articular facet of the twelfth dorsal vertebra from behind. Proper removal of the cartilage

of these facets in the fusion operation of the spine may be accomplished properly only after the removal of the mammillary process of the twelfth dorsal vertebra. This can be done after proper exposure, with a narrow osteotome, as shown in Fig. 8. It is believed that the omission of this operative step is responsible for occasional nonunion in this area, when an arthrodesis of the articular facets is performed.

SUMMARY

A study of the anatomic, functional, and surgical importance of the mammillary process of the twelfth dorsal vertebra was made. The process was found to be large and prominent on the twelfth dorsal vertebra. On the articulated spine it concealed the joint betwen the superior articular process of the twelfth and the inferior articular process of the eleventh dorsal vertebrae. A similar mammillary process was found on the last thoracic vertebra of the gibbon. The size and relation of the mammillary process were shown to present a good localization point for the twelfth dorsal vertebra in surgery of the spine. In spine fusion operations, involving the eleventh and twelfth dorsal vertebrae, a resection of the mammillary process of the twelfth vertebra is necessary for proper exposure of the joint between these two vertebrae.

I wish to express my gratitude to Dr. S. L. Washburn for valuable suggestions and the use of his excellent collection of gibbon skeletons, to Dr. H. Shapiro of the American Museum of Natural History, for placing at my disposal a collection of human skeletons, and also to the staff of the Department of Anatomy of the College of Physicians and Surgeons, for much appreciated help.

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TRAUMATIC OSTEOCHONDRITIS OF THE PATELLA

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WHEN a direct blow to the patella is received, the patella is driven against the adjacent femoral condyle and a greater or lesser degree of compressive force exerted upon the subchondral bone. This causes the development of areas of necrosis in the subchondral bone of the patella and femoral condyles which can be considered in almost the same light as a fracture. According to Bozan[1] the necrosis of bone may be attributed to the fact that the "minute girders of cancellous structure break at places predetermined by 'the laws of mechanics.' The broken mass of trabeculae interrupts the flow of blood and causes necrosis of certain predetermined segments." If the initiating trauma is mild and the amount of damage to subchondral bone minimal, spontaneous absorption and repair of the involved bone may occur. If, however, the area of necrosis in subchondral bone is more extensive, the area of involved bone is walled off and becomes a true sequestrum. Immediately, gross interference with the nutrition to the overlying articular cartilage layer develops, and consequent degenerative changes in that cartilage begin to appear. When these changes persist for a period of time, thinning of the articular cartilage of the patella, irregularities in contour, and fissures may occur. As a later manifestation, the synovium of the knee joint becomes irritated. In response to this irritation hypertrophy of the synovium and a chronic effusion result. Should the lesion remain untreated for a period of years, progressive arthritic changes in the knee joint will be found.

The lesion is certainly not uncommon. Darrach[2, 3] states that the articular cartilage of the patella showed evidence of chondritis in 36 cases out of a series of 157 arthrotomies performed for internal derangement of the knee joint. Chaklin[4] reported a series of 159 arthrotomies in 38 cases of which changes involving the articular cartilage of the patella and femoral condyle were discovered. Six examples of this condition have come to my attention.

REPORT OF CASES

CASE 1.—G. P., a white woman, aged 28 years, was admitted to Charity Hospital in New Orleans, Nov. 18, 1940, because of constant pain on weight-bearing for about eight weeks.

The patient had sustained an injury to the knee on three separate occasions, the first in 1928, the second a year later, and the last about two months before admission.

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She complained of some pain over the femoral condyles. Examination revealed slight effusion within the knee joint. Slight crepitation was elicited upon motion of the patella over the femoral condyles, but this motion did not produce pain. The most severe pain was felt when the examiner manually attempted to dislocate the patella laterally. There seemed to be a definite increase in the lateral mobility of the patella.

A diagnosis of recurrent dislocation of the patella and chronic synovitis was made. Nov. 20, 1940, the right knee was explored through a median parapatellar incision. When the joint was opened, a moderate amount of yellowish joint fluid escaped. Extensive synovial changes were apparent. There was definite synovial thickening and hypertrophy. The most striking changes were seen on the underside of the patella. Extensive fissures were present; there was widespread degeneration of cartilage and the process was diffuse.

Cross section of the entire patella showed an extensive area of fibrillary degeneration of the articular cartilage, the direction of which was at right angles to the articular surface. The cartilage showed longitudinal splits and wrinkles and the cartilage cells around these ''fractures'' had disappeared leaving an acellular matrix. Beneath this area the zone of intermediate calcification was absent and the subchondral area showed fragments of necrotic bone and cartilage present as loose masses filling the trabecular spaces. No definite line of infiltration of the subchondral plate could be seen in this section. This was probably due to the plane in which the section was cut. However, in every other respect the appearance was typical of osteochondritis.

While the patient was in the hospital a malignant breast tumor was discovered. Approximately one year later, she died from widespread pulmonary metastasis. During the interval when activity was possible, the knee gave no symptoms.

Case 2.—A. T. T., a white man, aged 36 years, was admitted to Charity Hospital in New Orleans, July 3, 1941, complaining of pain on weight-bearing and a ''snapping'' or ''locking'' in the knee. He had been using crutches since sustaining an injury to his right knee about one year before when he fell off a hay wagon. The internal semilunar cartilage was removed at another hospital. He was unable to state whether or not the cartilage was damaged. The symptoms persisted following the operation. Examination revealed findings similar to those in Case 1.

A preoperative diagnosis of internal derangement of the right knee joint, probably a remnant of the internal semilunar cartilage, was made. July 9, 1941, through a median parapatellar incision the right joint was explored. The gross pathologic findings at operation were characteristic of this condition. The patella was completely excised, and the defect in the patellar tendon repaired with interrupted cotton sutures.

Aug. 8, 1941, the patient was ambulatory with motion in the right knee from an angle of 180 degrees in extension to 90 degrees in flexion. The ''snapping'' and ''catching'' sensations in the right knee had completely disappeared.

Case 3.—D. M. V., a Negro woman, aged 21 years, came to Charity Hospital in New Orleans, Oct. 23, 1941, because of vague pain and swelling in the right knee and a sensation of occasional ''catching of the knee.''

Two years prior to entry, the patient struck her right knee forcibly against a washtub. There was no immediate disability, but within a week the knee became greatly swollen and extremely painful.

The patient walked without a limp. Palpation revealed slight thickening of the synovium. There was an increase in the amount of joint fluid, but no ballottement of the patella was possible. Complete flexion and extension of the knee could be accomplished, but slight pain was felt upon extremes of motion. Passively, motion of the patella was free, but there was a palpable grating sensation as the patella was moved over the femoral condyle, and some slight pain was produced. Circumferen-

tial measurements showed one-quarter inch atrophy in the right thigh. Laboratory findings were negative. Roentgenograms showed slight atrophy of the injured patella as compared with the normal side. On the lateral view there appeared a slight area of decreased density on the lateral femoral condyle which shaded into normal density at the periphery. No significant changes could be made out in the contour of the patella itself.

A preoperative diagnosis of chronic synovitis of the right knee of unknown etiology was made. Nov. 5, 1941, the knee joint was opened through a median parapatellar incision. The findings at operation were similar to those in Case 1. The patella was excised and the defect in the patellar tendon repaired with interrupted sutures of cotton.

After six weeks this patient failed to return to the clinic. Efforts to locate her for examination were in vain.

CASE 4.—R. S., a white male, aged 20 years, was seen in Charity Hospital in New Orleans, July 14, 1940, with a slipped femoral epiphysis on the right side, which was several months old. July 20, 1940, an osteotomy through the neck of the femur was done and a Smith-Petersen nail inserted to maintain fixation. Shortly after the beginning of active exercises an effusion appeared in the right knee joint. No history of injury was elicited. The effusion was not present when the patient was first seen nor on any subsequent admission. Because the effusion was considered to be transitory and related to the physical therapy, the patient was allowed to return home wearing an ACE bandage support.

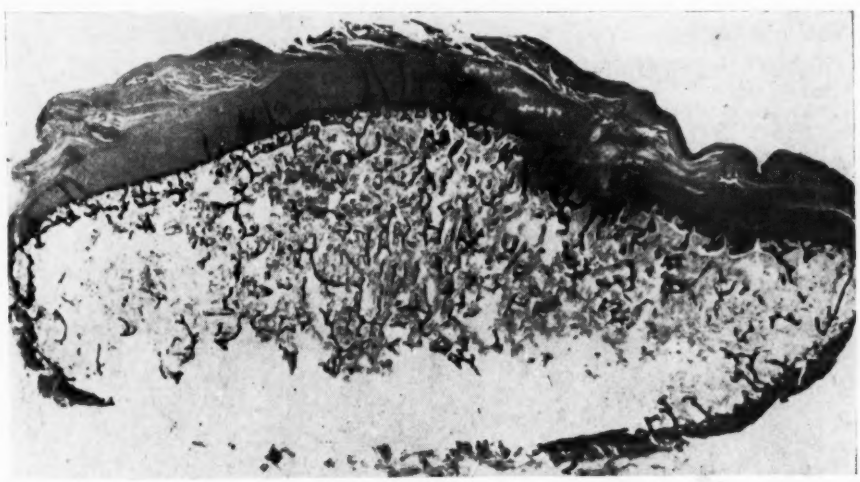

Fig. 1.—R. S., Case 4, shows fibrillated and degenerated cartilage with changes in, and infiltration of, subchondral bone; nontraumatic in origin. Compare with Fig. 2.

He was readmitted to the hospital, March 17, 1941, at which time the effusion in the right knee was still evident, but the patient had no complaints. Aspiration of the fluid in the right knee showed a clear yellowish material, with normal cell count and no growth on culture. Following aspiration a definite grating sensation was noted with motion of the patella over the femoral condyle, but this was only slightly painful. Roentgenograms of both knees showed nothing in the patellar region aside from the effusion.

A preoperative diagnosis of osteochondritis of the patella was made, and on March 27, 1941, the knee joint was opened through a median parapatellar incision. The operative findings were identical to those of Case 1. The patella was excised, and the defect in the patellar tendon repaired with interrupted sutures of black silk.

Microscopic examination of the excised patella revealed the following (Fig. 1). Section through the articular cartilage showed considerable fibrillary degeneration of the superficial portions. There was also an irregular overgrowth of degenerated fibrocartilage. In one area the osteochondral junction was disrupted and the connective tissue invaded rather deeply into the underlying bone with resorption of trabeculae. There was an irregular deposition of new bone. Portions of the osteochondral junction were fairly regular in appearance. The periosteal surface of the bone also showed fibrous thickening. There was considerable splitting of the overgrown peripherally located fibrocartilage. Sections through the synovial tissue revealed swelling of the synovial mesothelium and perivascular mononuclear and plasma cell infiltration of the capillaries and the underlying connective tissue.

Nov. 6, 1941, the patient was working in a lumber mill as a laborer without disability referable to the knee joint and without evidence of recurrence of the swelling or effusion.

CASE 5.—L. S., a Negro woman, aged 44 years, was admitted to Charity Hospital in New Orleans, March 20, 1942, because of pain and swelling in the right knee. A direct blow over the right knee sustained in July, 1941, resulted in swelling and pain in the knee joint.

On examination some thickening of the synovium was noted and there seemed to be an increase in the amount of joint fluid. The patella was freely movable with some pain in the region just lateral to the patellar margin on its medial and lateral borders. A palpable grating sensation was present upon motion of the patella over the femoral condyles. There was free motion in the right knee from 180 degrees in extension to 40 degrees in flexion. No measurable atrophy was found in the thigh or calf.

A preoperative diagnosis of osteochondritis of the patella was made, and on March 25, 1942, the knee joint was opened through a median parapatellar incision allowing the escape of a moderate amount of clear yellowish fluid. Operative findings were characteristic of traumatic osteochondritis. The patella was excised and the defect in the tendon repaired with interrupted sutures of cotton.

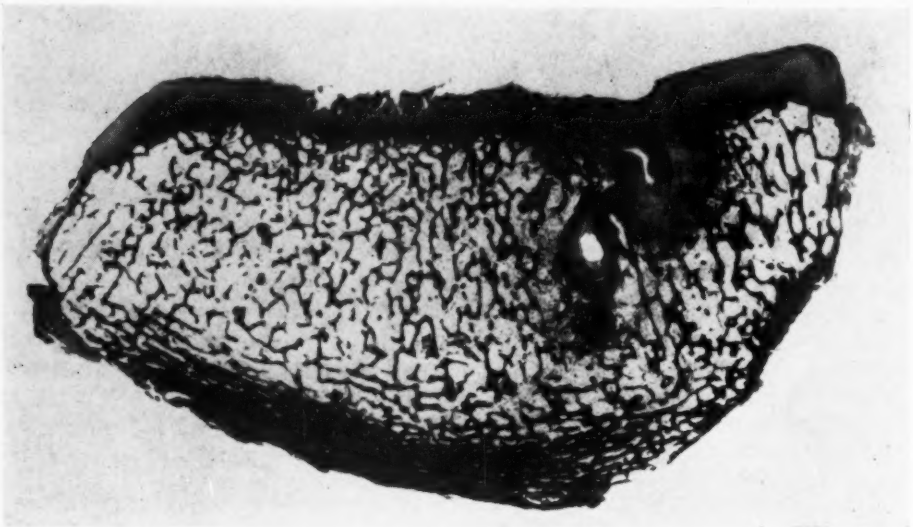

Fig. 2.—H. K., Case 6, shows extensive degeneration of articular cartilage with destruction of subchondral bone; definitely related to trauma. Microscopic picture identical with Fig. 1.

CASE 6.—H. K., a white female, aged 17 years, was complaining of pain in the right knee when she was admitted to the Hospital for Ruptured and Crippled in New York, Nov. 7, 1939.

About two and one-half years before admission, the patient struck her right knee forcibly against the cement surface of the walk when hit by an automobile. The knee continued to be painful and disabling for eighteen months. Conservative treatment was not beneficial.

Physical examination showed a low-grade effusion, some slight thickening of the synovium, and pain with extreme flexion or extension of the knee joint. The right thigh measured 2½ inches less than the left. Crepitation and pain were produced with passive motion of the patella over the femoral condyle. The roentgenograms showed slight effusion into the joint and generalized atrophy, but no distinctive changes in the patella or adjacent femoral condyle.

Nov. 11, 1939, the right knee joint was opened through a median parapatellar incision. Pathologic changes observed at operation were identical to those in the other cases. The patella was excised.

Microscopic examination of the excised patella (Fig. 2) revealed considerable degeneration of the articular cartilage. The cells in many places showed no tendency to absorb stain at all. In the periphery the cartilage appeared well vascularized and much more cellular. Areas of necrosis in the underlying bone with evidence of attempted repair were noted.

In February, 1941, the patient stated that her right knee was comfortable. There was a normal range of motion. Some atrophy of the thigh musculature persisted, but the symptoms experienced before operation had completely disappeared.

DISCUSSION OF CASES

In all cases except one a direct injury to the patellar region was sustained which forced this bone against the anterosuperior surface of the medial femoral condyle. This resulted in immediate temporary disability, caused by local swelling and pain upon flexion or extension of the knee joint.

The acute symptoms referable to the knee joint subsided for several weeks or months. With the passage of time there appeared a low-grade chronic effusion, which fluctuated in degree with the extent and character of exercise indulged in by the patient. Definite vague symptoms of discomfort persisted within the knee joint and vague pain was felt on its anterior aspect. This sometimes was made worse by exerting strain upon the flexed knee through the quadriceps apparatus, as when kneeling or squatting. All patients complained of occasional symptoms of "locking," or "catching," which may simulate the condition commonly referred to as an internal derangement of the knee joint. The condition is a chronic one as evidenced by the fact that the average duration of symptoms in the present series (excluding the case with a history of twelve years) was 13.2 months.

The physical findings in this group of cases were typical. There was definite effusion within the knee joint; in some cases it was minimal and in others, grossly apparent. Thickening of the synovium was usually palpable. Mild pain referred to the anterior compartment of the patella was felt when the knee was acutely flexed or extended. Atrophy of the thigh varied with the severity of the symptoms produced by the lesion.

Crepitation, or "grating sensation," could be elicited upon passive motion of the patella over the articular surface of the femoral condyles. Pressure over the patella or passive motion of the patella caused pain. Occasionally, this could not be clearly demonstrated until the excessive joint fluid was removed by aspiration. Synovitis and obliteration of the suprapatellar pouch shadow by an intra-articular collection of fluid were seen in the roentgenograms but were so minimal as to be almost insignificant in most cases. Fig. 3 shows two views of the patella taken after excision. The only changes which can be seen are in the patella. These would not be visible in the routine films made preoperatively. Suggestive atrophy of the patella and femoral condyles can be seen in the film, but this is not of much diagnostic value.

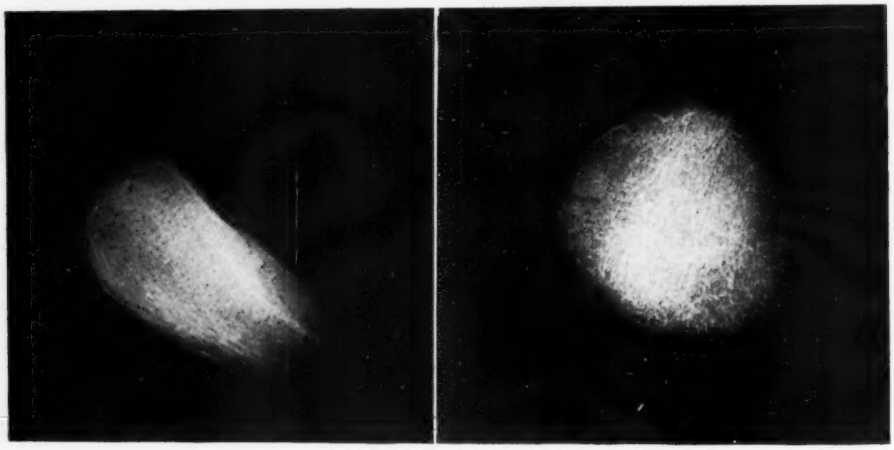

Fig. 3.—Anteroposterior and lateral views of an excised patella, showing no significant changes visible in cancellous bone. The microscopic sections of this patella are shown in Fig. 1.

The following gross pathologic changes were noted at operation: (1) softening, irregularity in contour, and fissure formation in the articular cartilage of the patella; (2) yellowish discoloration of the articular cartilage in the areas of involvement; (3) similar changes in the articular cartilage of the femoral condyle on its anteromedial aspect; (4) thickening, hyperemia, and villous degeneration of the synovium, usually confined to the suprapatellar pouch region and the anterior compartment of the knee joint; (5) increase in amount of joint fluid, usually clear yellow in color with normal cell count, or slight increase in polymorphonuclear cells; (6) pannus formation at the edges of the articular cartilage of the patella and femoral condyles.

COMMENT

The changes which occur in articular cartilage as a result of direct trauma have been recognized for many years. First described by Budinger[5, 6] in 1906, it was later clarified by Konig[7] and Laewen.[8] Attention has always been directed toward the cartilaginous changes, and

the syndrome produced has been referred to as traumatic cartilage fissuring (Budinger, 1906), chondromalacia (Konig, 1928), and chondritis (Darrach, 1935). Kulowski,[9] Slowick,[10] Herzmark,[11] Darrach,[3] and Chaklin[4] have all referred to the syndrome in the American literature. They ascribed the etiology to trauma and particularly emphasized the changes which were found in the articular cartilage. In my opinion the true pathologic change is to be found in the underlying cancellous bone, and the change in the articular cartilage is an entirely secondary one.

The one point of interest in the present series which cannot be properly interpreted is that absolutely no history of injury was elicited in Case 4. The patient was convalescing from an osteotomy for slipping of the upper femoral epiphysis. While the patient was still in plaster, an osteochondritic focus developed in the patella of the same extremity. The histologic picture of the excised patella in this case was almost identical to that of the other cases reported. Trauma must certainly be considered as the prime cause of this particular type of osteochondritis dissecans although we cannot conclude that it is the sole cause.

In almost every case that I have studied, or that has been reported by others, uniformly definite inflammatory changes developed in the synovium of the knee joint. In this series the synovitis was localized to the anterior compartment of the knee joint and associated with hypertrophy and thickening of the infrapatellar fat pad. Pannus formation was observed over the involved femoral condyles and the edge of the articular surface of the patella. In every instance there was evidence of the persistence of chronic synovitis, and progression of the extent of involvement of the synovium with the passage of time. If these changes exist for a long time, osteo-arthritic changes will develop. This fact is clearly brought out by a review of the available literature.[5-10, 12] Laewen[8] in 1925 reported thirteen cases and considered the removal of the injured cartilage as an early operation for arthritis deformans. Key[12] in 1924 emphasized that contusion of cartilage could lead to chronic progressive arthritic change. Bozan[1] attempted to explain this phenomenon in his statement, "Due to the accepted fact that these foci are aseptic, all too complete innocuity is attributed to them. Necrotic tissue, even if aseptic, elicits reaction from its surroundings. The reaction is not violent and consists mainly of edema. The edema pervades the surrounding soft tissues, increases the amount of joint fluid, and leads to spasm, stiffness, and pain." The process may be much more complicated than this. In the present group of cases, where changes were noted in the articular cartilage of the femoral condyle, this area was not disturbed. Only the patella was removed. In four instances, therefore, degenerated fibrillar cartilage was allowed to remain within the joint and if areas of aseptic necrosis in the cancellous bone of the femur existed, these were also allowed to remain. However, every one of the six patients treated by excision of the patella, with the

synovium and degenerated femoral cartilage left undisturbed, made complete recoveries, with disappearance of the synovitis and effusion in every instance. Some other factor may well be the cause of the late development of arthritic change. Removal of the involved cartilage alone has caused subsidence of the synovitis and secondary joint changes. Patellaplasty has given good results, although apparently not quite as good as patellectomy. In earlier cases with minimal changes perhaps simple resection of the involved cartilage will suffice; however, in the more severe grades with complete erosion of the cartilage it is believed that patellectomy is preferable. The fact is recognized that recently arthritic changes have been shown to develop following patellectomy in the rabbit.[13] It is known that arthritic changes will develop if the patella is allowed to remain in situ under the present disease process in man. I am not completely convinced that removal of the patella in the human being will lead to arthritic changes in later life. Although there is no definite proof at this time, it is felt that the more severe and permanent changes resulting from an osteo-arthritis have been obviated in this group by removal of the patella. The lesion, as described, is rare by admission, but perhaps not so rare as it might seem at first glance. If the undersurface of the patella were routinely inspected in every exploratory operation for internal derangement of the knee joint, probably more cases would be encountered.

CONCLUSIONS

1. Diffuse osteochondritis of the patella can result from trauma.
2. The lesion causes a minimal amount of disability, but a real one.
3. The history is fairly typical, the symptoms chronic.
4. The physical findings are negligible.
5. If untreated for a period of years, the lesion would probably lead to irreparable damage caused by superimposed osteo-arthritic changes.
6. If symptoms persist, patellectomy will result in complete disappearance of the synovial inflammatory changes, and absolute alleviation of symptoms. By inference, it should prevent the development of osteo-arthritis in later life.

The author wishes to express sincere thanks to Dr. Phillip D. Wilson and Dr. Dominic De Santo of the Hospital for Ruptured and Crippled in New York City for arousing an interest in this subject and furnishing Case 6 of this series for study; to Dr. Guy A. Caldwell and Dr. R. H. Allredge of the Tulane University School of Medicine for allowing him to continue this study to its present point.

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TREATMENT OF TENDONS IN FINGER AMPUTATIONS AND DESCRIPTION OF A NEW INSTRUMENT

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DISPOSITION of severed tendons in finger amputations is a matter on which there is some diversity of opinion. The teachings of most published works on operative surgery recommend some form of suturing the tendon ends to the tendon sheath or to the bone in order to preserve the greatest function of the fingers.

Kirk[4] advocates the following procedure for a metacarpophalangeal disarticulation: "The finger is hyperextended and flexor tendons cut and allowed to retract in their sheaths. The finger is flexed, the extensor tendon cut, and with a small, sharp-bladed knife the joint is opened, the capsular ligament cut around and the finger removed."

This hyperextension of the finger, allowing the flexor tendons to retreat in their sheaths, gives a very useful hand. Attempts to secure the tendons to the sheaths at the point of division of the tendon, or even worse, suturing the flexor to the extensor over the end of the metacarpal stump, produces an unusual type of disability, with loss of the grip and inability to flex the fingers into a tight fist (Figs. 1, 2, and 3).

The mechanism of this disability is interesting and is related to the common origin of the flexors, particularly the profundus group, so that tension on any one tendon restricts, partially, the excursion of the others. This is best demonstrated in the normal hand by holding one's middle finger straight in line with the metacarpals, then trying to close the other fingers into a tight fist. The fingers cannot be entirely closed, and there is pain in the forearm and hand as this is attempted.

In amputations through the proximal phalanx, it is common practice to suture tendons to tendon sheath. This is satisfactory if the finger is hyperextended before the tendon division, but it is unnecessary for finger function and occasionally results in disability if the tendons become adherent while under slight tension. The difference in excursion of the sublimis and profundus tendons has been accurately measured by Bunnell[2] and consideration of this difference makes illogical the suturing together of both tendons in the sheath.

It is better practice to allow the tendons to retract within the sheath, or if they are densely adherent, as from an old injury, both profundus and sublimis should be stripped out to allow free motion (Figs. 1, 2, 3, and 4). Control of the proximal phalanx is exercised through the

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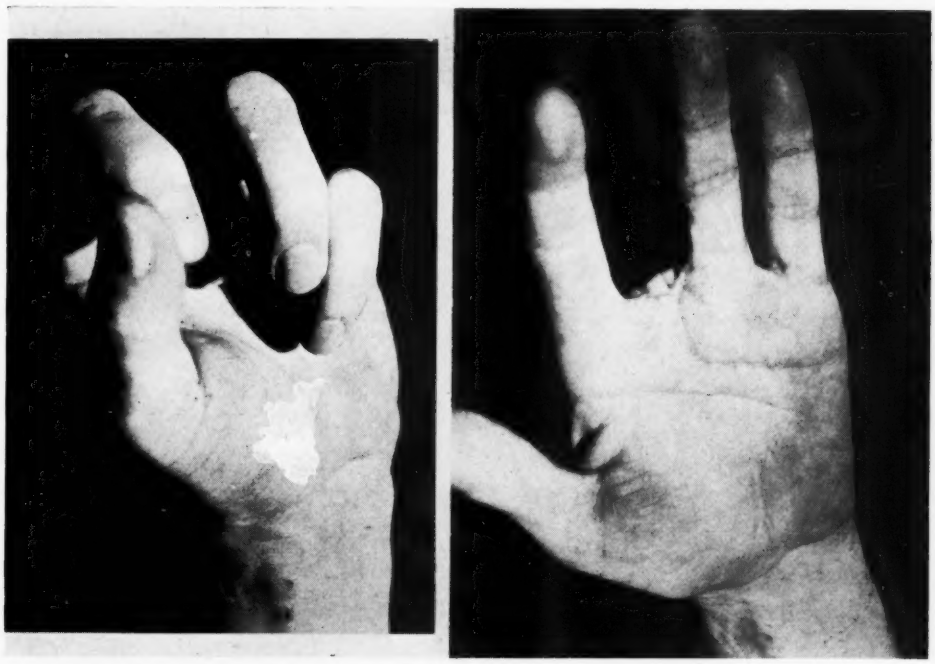


Fig. 1.—Disability produced by suturing flexor sublimis and flexor profundus tendons of the middle finger to the extensor tendon over the distal head of the metacarpal in a metacarpophalangeal disarticulation. Patient cannot close fingers to make a fist and cannot extend them completely.

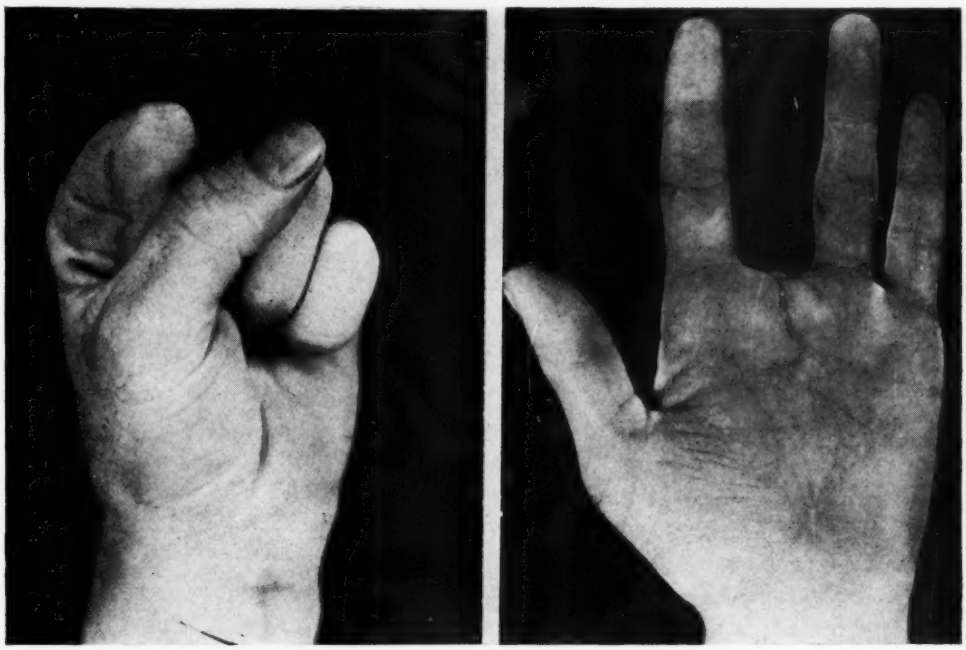


Fig. 2.—Same patient as shown in Fig. 1 after total excision of flexor sublimis and flexor profundus tendons. Note the small transverse scar at the wrist through which proximal ends of tendons were severed. Full function is present.

digital extensor complex, which has been described in minute detail elsewhere.[9] Essentially, this extensor complex, composed of lumbricals and interossei, acts as a flexor of the proximal phalanx when it passes volarward beyond the midline of the flexion axis of the metacarpophalangeal joints. The interossei, which carry the greatest load in this motion, are very strong and give an excellent grip.

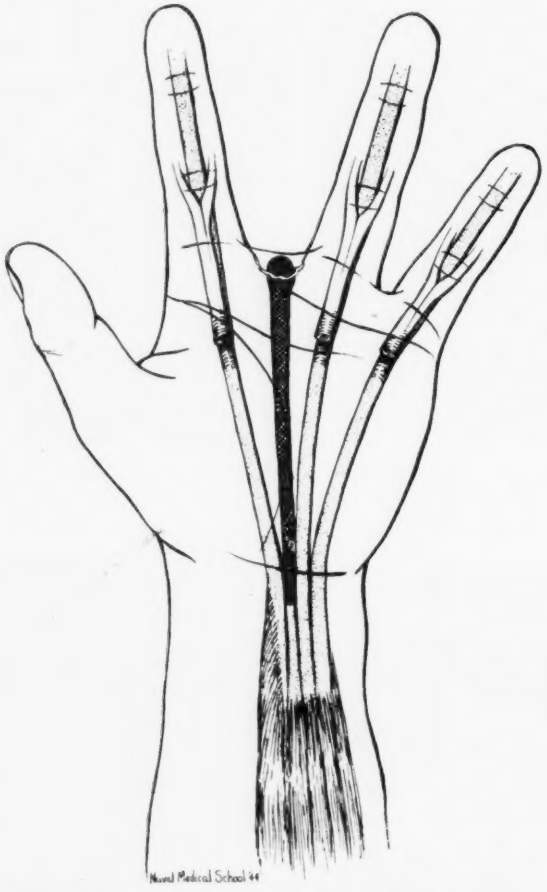


Fig. 3.—Schematic drawing, showing position of tendons excised (black, crosshatched area). The common origin of the flexors illustrates the reason for the disability shown in Fig. 1.

Disarticulations at the distal interphalangeal joints or amputations in the middle phalanx are best treated by dividing the flexor profundus tendon and allowing it to retract (Fig. 5). This practice has been amply supported by Stevenson[8] and others and gives a better grip than does suturing the tendon to the sheath.

Amputations in the terminal phalanx rarely involve tendon division, for if they are distal to the tendon insertion in the buttonlike base of the terminal phalanx, the tendinous attachment is left intact. Reattachment of the severed flexor profundus insertion should be carried out if avulsion has occurred.

Extensor tendons do not retract appreciably and if left alone will become adherent to the underlying bone, and function quite well. Here, of course, there is no problem of any tendon sheath. In the thumb, tendons should be preserved and sutured to the bone with tension as nearly normal as possible.

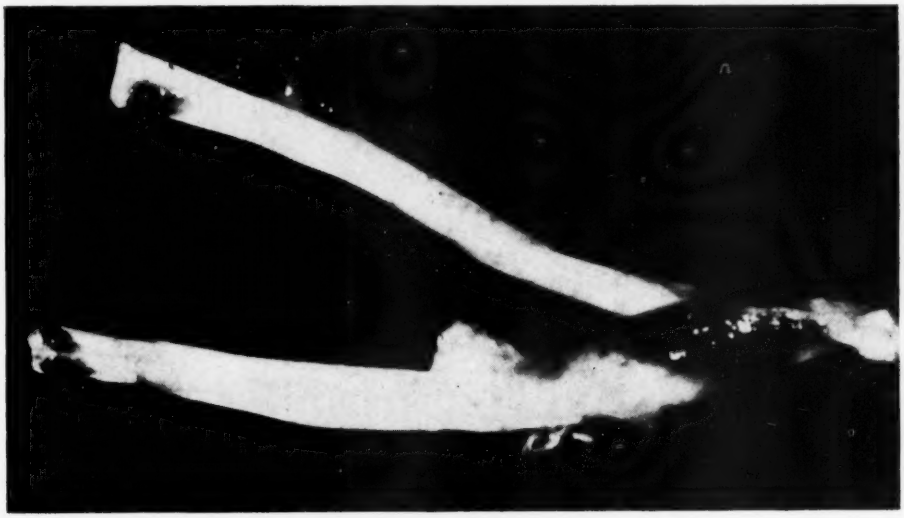


Fig. 4.—Specimen obtained at surgery. The lumbrical muscles are still attached to the flexor profundus tendon.

Fig. 5.—Recently healed traumatic amputation of ring finger in which flexor profundus tendon was cut and allowed to retract. There is excellent function of the stump and of the other fingers.

AMPUTATIONS IN CONTAMINATED OR INFECTED CASES

Although the foregoing discussion has applied to clean cases, it is frequently necessary to amputate a digit in the presence of contamination from immediate trauma. In exceptionally clean cases, the tendons can be allowed to retract, but where contamination is excessive in very dirty wounds, or where blood supply has been impaired or tendons fragmented, the possibility of spreading infection more proximally in the hand must be borne in mind. In such cases and in frankly infected cases, the tendon or tendons should be sutured to *one side* of the tendon sheath, securing it against retraction, and leaving the remainder of the sheath *open* for drainage.

Function following such procedures may or may not be good, depending on the location of the tendon division and the tension on the tendon stump. Whatever the resulting function, it is secondary in importance to maintenance of integrity of the protective barriers against bacterial invasion, and function can be dealt with later when the wounds are well healed. Fragmented tendons are excised or trimmed back to viable tendon, all foreign particles are removed, and copious saline irrigations are used to wash away unseen debris. Sterile normal saline dressings are applied at the operating table and continued while the patient is in the ward in those cases where primary closure is not elected.

LATER RECONSTRUCTION SURGERY

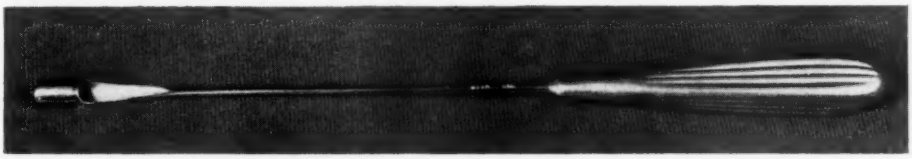
When the destructive phases of infection have passed, masses of dense scar restrict movement and bind tendons, sheaths, and surrounding tissues into a functionless inelastic cicatrix. In an intact finger, tendons may be freed from scar and attempts made to restore the delicate gliding mechanism, usually by a free tendon graft, as advocated by Mayer,[7] Bunnell[1] and Mason,[5] and now almost universally employed. Mayer[7] stated that "In old cases, it is wise to excise the scarred remnants of tendon entirely and replace with a free graft of tendon sheath."

In an amputated finger, however, it is rarely, if ever, advisable to put in a new tendon, or repair the old, and excision of the scarred flexors in their entirety gives a better functioning stump. With amputation distal to the insertion of the flexor sublimis digitorum, an attempt should be made to preserve the sublimis tendon and strip out the profundus. A free graft of long-fibered sliding fat from the lateral thigh or triceps tendon regions, as advocated by Bunnell, is most useful in this connection, implanted about the rough tendon to restore its gliding mechanism. A pedunculated flap of fat, as suggested by Kanavel,[3] would not be a practical procedure in an amputated digit.

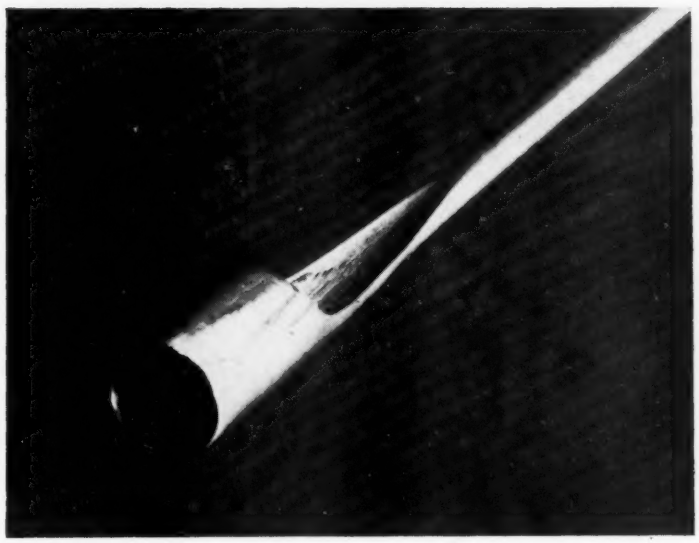
A NEW TENDON STRIPPER

The removal of a densely adherent tendon from its scarred bed would require extensive incisions in the hand if one sought adequate exposure

of its entire length. Excision through small transverse incisions in the hand and wrist can be carried out nicely with smooth tendons which strip easily from normal surrounding tissues. An adherent tendon must be freed and a ringlike stripper has been designed (Fig. 6) with a long thin handle to dissect such adhesions and free the tendon in much the same manner as Masson's fascia stripper[6] is used to remove long strips of fascia lata through a small incision in the thigh. The tendon can then be severed through a second small transverse incision in the wrist (Fig. 2), obviating the need for the double-tubed sleeve-cutting device of Masson.



A.



B.

Fig. 6.—*A*, Author's instrument for stripping adherent tendons in the palm when one end of the tendon is severed, as in a finger amputation *B*, Close-up of cutting tip of stripper.

Bunnell[1] developed tendon strippers many years ago and they are in general use today. His development of the stripper was for a slightly different purpose at that time. He states that: "When a tendon that is imbedded in adhesions is freed, the surface of the tendon is usually very ragged and hacked. To avoid this, it is well to use the tendon stripper to be described further." Later he describes their construction originally from a set of nested cork borers.

The slotted stripping sleeve of the Bunnell stripper allows its application to an intact tendon, both ends of which are attached. The stripper

described herein for excision of tendons in an amputation stump is fitted over the severed end of tendon and is guided through the palm on the tendon. In this manner, chance slipping of the cutting edge during sometimes vigorous division of adhesions cannot occur and injury to important nerves and vessels in the palm is thus prevented.

SUMMARY

Flexor tendons need not be sutured to bone or tendon sheath in clean cases and must not be overlapped and sutured over the end of the bone to the extensor tendons. Disability, with weakness of the grip, results. In contaminated or infected cases, they should be anchored at the point of amputation and the tendon sheath left open to avoid spread of infection to the hand. Such tendons may become adherent and produce disability. They should be excised to free the finger, relying on the intrinsic muscles of the hand for motion of the stump. A tendon stripper, suitable for freeing such tendons in the hand, is described.

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MODIFIED CALIBRATED SKIN-GRAFTING KNIFE

Further Observations

Major Kerwin M. Marcks, Medical Corps, U. S. Army

I AM presenting this paper as a supplement to a recent article* describing a modified calibrated skin-grafting knife. Reports of the use of this knife have been very encouraging. Personal communications from Kilner in London, Doud in the European theater of operations, and surgeons in this country have described gratifying results. In my previous paper I neglected to advise as to the method of using the knife, and shall attempt to rectify this by giving a few simple instructions.

The size of the graft to be cut will depend on the surface area of the donor site, the amount of skin required, and the ability and patience of the operator. For skin traction I prefer the Blair-Brown suction cups, with the assistant holding a board for countertraction. A board or pan can be used, however, in the place of the suction cups to keep the skin as level as possible, and also on slight tension. Petrolatum jelly is then applied to a previously prepared donor area. The attachment is regulated according to: (1) the thickness of skin desired; (2) the area from which the graft is to be taken; (3) the age of the patient; and (4) the condition of the skin. The knife is placed flat and firm on the skin, but not with too much pressure, and a sawing motion is begun. The rod should remain stationary during the cutting of the graft, except for its rolling motion, with the graft presenting between the rod and the blade and rolled up over the blade of the knife, as illustrated in Figs. 1 to 7.

Tilting the knife away from its parallel position might increase or decrease the thickness of the graft and cause the rod to move with the knife. This defeats the purpose of the thickness-determining factor and should be avoided. Should the graft be too thick or too thin, correction is made by adjusting the thickness-regulating screws. The adjustment can be readily accomplished without removing the knife from the donor site, simply by turning the screws clockwise to increase the thickness of the graft and counterclockwise to decrease the thickness of the graft. When the cutting is completed, the graft is placed between layers of warm saline gauze, and the donor area is dressed according to the usual custom of the operator.

The care of the knife after cutting the graft is important. A sharp knife is essential, and it should demand the respect of the operator at all times. I present the knife to the nurse after using. She removes

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*Marcks, K. M.: Modified Calibrated Skin-Grafting Knife, Mil. Surgeon 92: 653, 1943.

the rod, washes it with warm water, and then with ether. She then places a small amount of petrolatum jelly on the blade, replaces the rod, and wraps the assembly in a towel. When the knife is to be used, I remove the rod and the attachment, wash with ether, and strop the blade with emery powder on a wet towel according to the directions of Blair and Brown for the care of the Blair-Brown knife. The knife is then wiped with the wet towel, dried, and the attachment replaced. It is placed in 70 per cent alcohol until ready for use, when it is washed with sterile water and dried with sterile gauze. Kilner uses a three-way strop and gets excellent results.

A.

B.

Fig. 1.—*A*, Microphotograph of section of skin cut with the assistant turning thickness-determining screws in order to increase the thickness of the graft while the graft was being cut. Knife did not leave skin during the cutting of the graft.

B, microphotograph shows self-adjustment while cutting graft. The thinner split graft was cut, the adjustment made at the central depression area, and then the thicker split graft cut without removing knife from skin.

Both these specimens were cut for slide demonstration purposes.

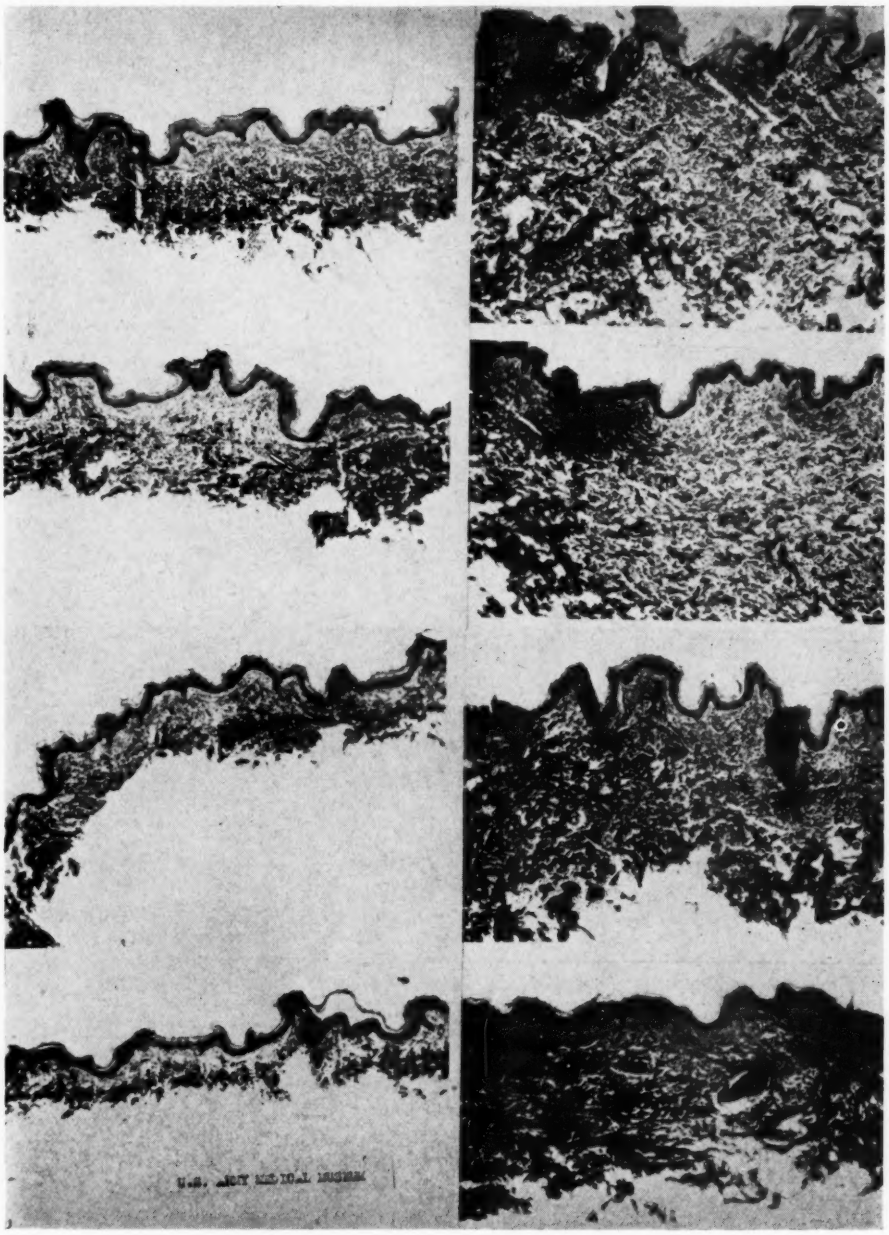


Fig. 2.—Microphotographs show various thicknesses of split grafts cut with the described modified calibrated skin-grafting knife.

A. *B.* *C.*

Fig. 3.—Illustration of the cutting of a split graft with the modified skin-grafting knife. The end of the procedure is seen in *B* and the donor area and graft *C*. The inside of the thigh, when available, is an ideal location for the cutting of a large graft and in my experience is more frequently used than any other donor site.

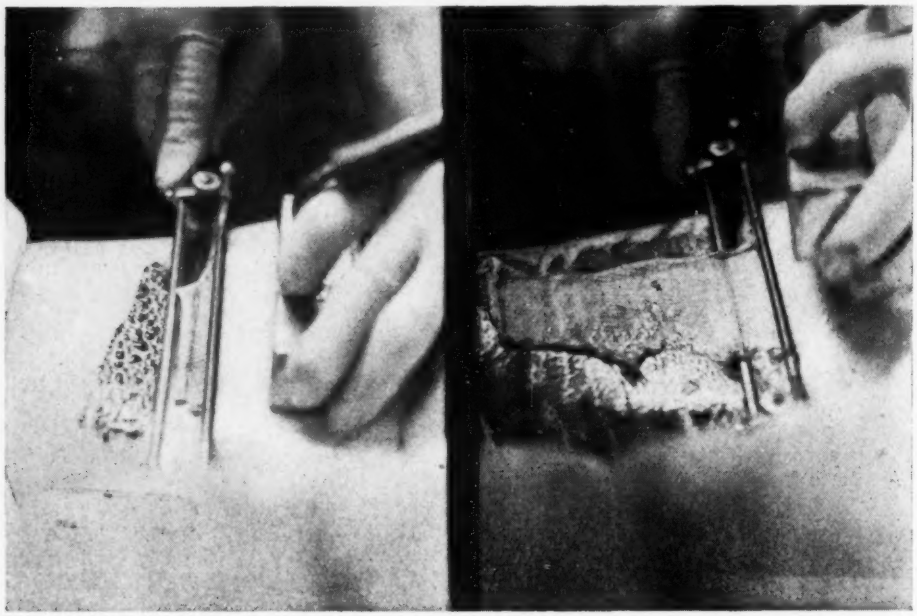
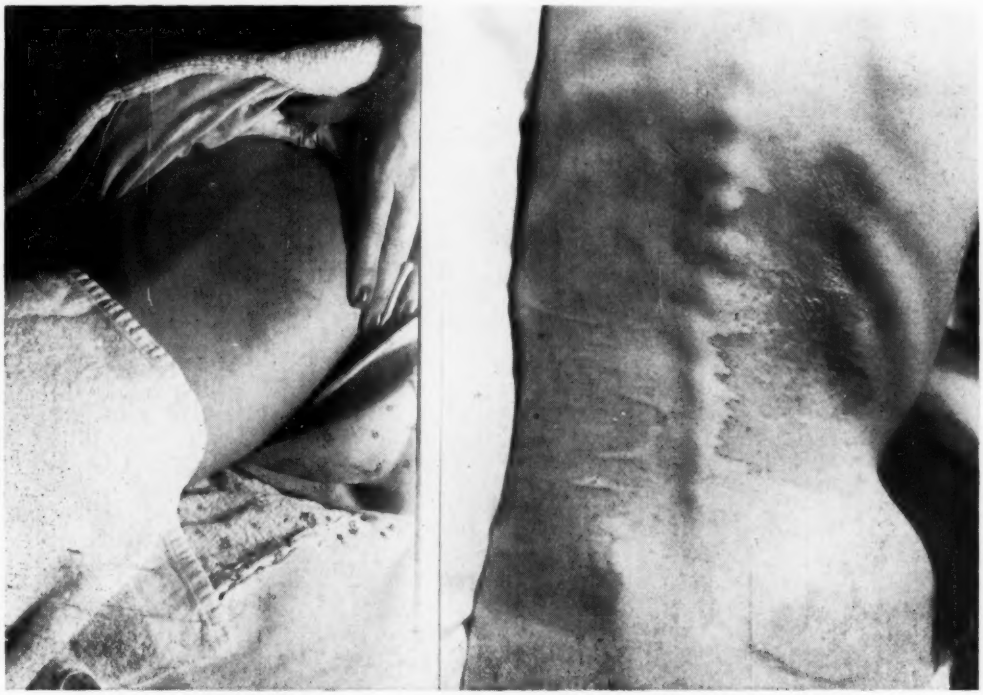


Fig. 4.—Illustration of the cutting of a thicker split graft from the thigh. Notice the amount of retraction of the graft as compared to the thinner graft in Fig. 3.

How often should the knife be honed? This is a difficult question to answer and must be left to the judgment of the surgeon. I have cut thirty-three grafts with one of my blades before I felt honing was necessary.

The cutting of a graft with this appliance should offer no difficulty if one is accustomed to the cutting of a graft with a straight blade. If one is not accustomed to cutting grafts, practice may be necessary. To determine the thickness to be cut, I simply hold the knife to the light to observe the space between the blade and the rod. However,



A. *B.*

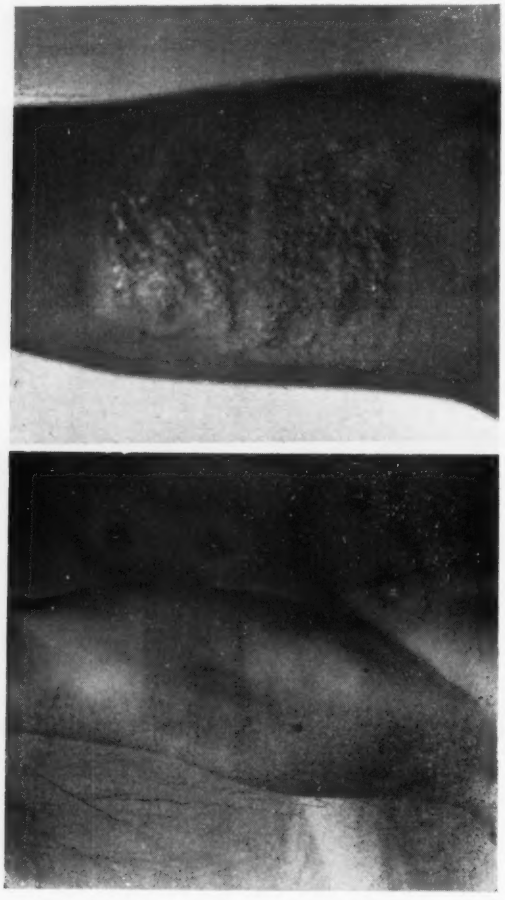
Fig. 5.—Donor areas on the back. Both of these patients had burns of the legs. The anterior and lateral surfaces of one thigh were used. A small split graft was still necessary to cover the granulating area on the posterior surface of one of the legs and the back was readily available as a donor site. In *B*, donor areas are shown on the back. The edges show a great deal more irregularity as compared to *A*, but the graft was placed on granulating surface and this factor was not important. An emaciated back like this may offer considerable difficulty in cutting a graft.

there are graduations which may be used to determine the thickness. For this purpose, the screw must be turned counterclockwise until the rod touches the blade. This will be the zero index. Then the screw must be turned clockwise to the desired number of graduations past the zero index necessary for a particular thickness of graft desired.

There is one difficulty that may arise in cutting the graft. A satisfactory graft may be cut with one end of the knife, but the other end may appear thicker in spite of equal calibration. In this case it might be

well to check the width of the blade because, if the blade is so wide that its edge lies opposite the center of the rod or extends beyond the center of the rod at either end, the disturbance mentioned will result. This can be corrected by sending the knife to the manufacturer for honing, so that the width of the blade is made equal throughout and so that, when the screws are turned down, the edge of the blade will strike the rod everywhere just proximal to the center of the rod.

A.



B.

Fig. 6.—Donor areas on the side of the upper arms. Notice the keloid formation on the donor area of the Negro patient (*A*). This is another convenient and practical donor site. Quite a wide graft can be cut from this region by having the operator place his foot on a stool, grasping the patient's arm and placing it across his thigh, thus resting the upper arm and increasing the surface area.

Finally, I wish to stress the importance of considering the age of the patient, location of the donor area, and condition of the skin from which the graft is to be cut, since these factors are variable. If good sound surgical and anatomical judgment is always employed, this instrument will serve a good purpose.

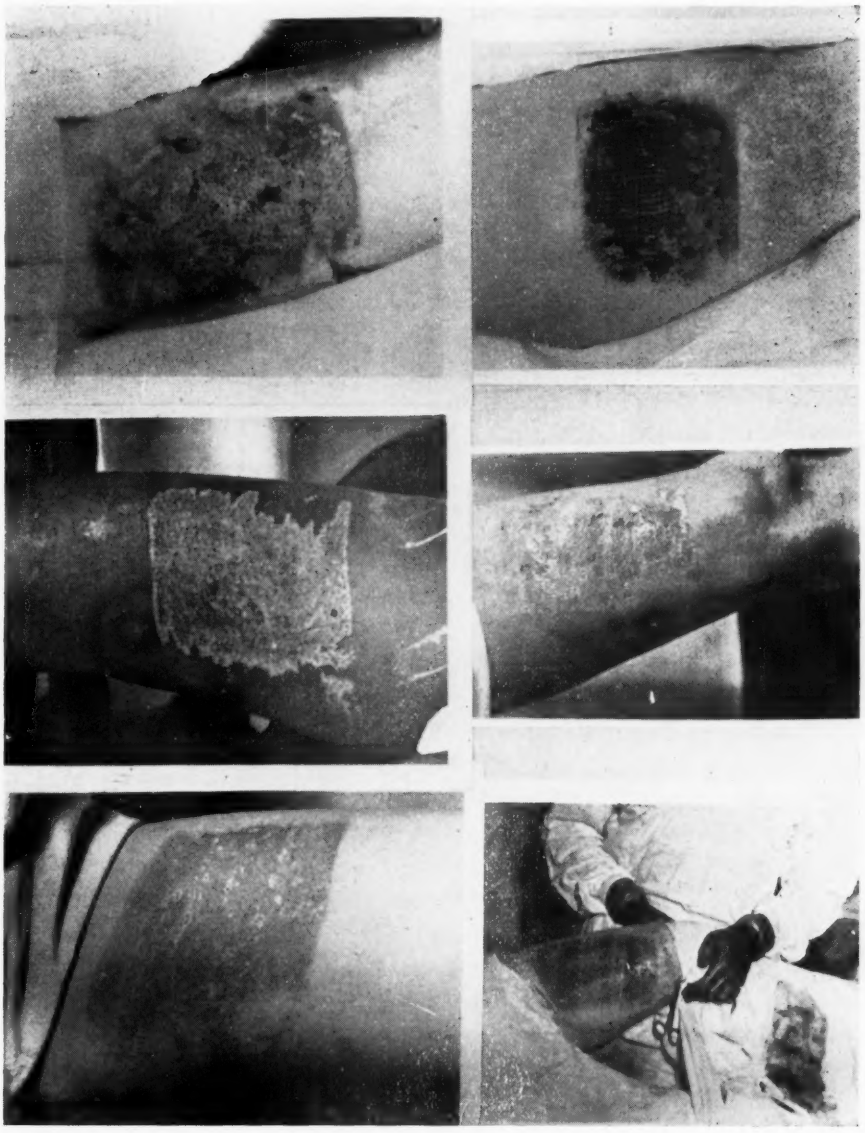


Fig. 7.—Donor areas on the inside thigh regions. As mentioned previously, the thigh is an ideal donor site and extremely valuable when a wide and long graft is necessary to cover an extensive denuded area. The edges of the donor areas are not always this regular when this knife is used but after practice, trial and error, and with a moderate amount of patience, a nicely shaped graft can be removed with the resultant donor areas as shown here.

SUMMARY

I have presented a supplement to a previous paper illustrating the use of the attachment to the Blair-Brown skin-grafting knife for the cutting of split grafts.

ANESTHESIA FOR THE BURNED PATIENT

CAPTAIN E. M. PAPPER, MEDICAL CORPS, ARMY OF THE UNITED STATES

BECAUSE of the large number of burns among the casualties of modern warfare, considerable interest has been manifested in the various aspects of the treatment of the burned patient. Extensive studies, experimental and clinical, have been presented on the problems of pathologic physiology and the clinical management of burns, with particular emphasis upon the control of plasma loss and shock with plasma replacement therapy, and also upon the factors concerned with the local treatment of the burned areas. Despite the interest in the problem of burns and the mass of material available for study, comparatively little attention has been paid to the importance of the anesthetic management of the burned patient who requires operative procedures either early or late in the course of the injury.

Generally speaking, the consensus has been that the surgical treatment of acute burns should be performed without anesthesia where possible.[1] However, there are many instances in which the employment of an anesthetic is necessary to the successful completion of a surgical procedure in the burned patient. In this connection pentothal sodium has been recommended by several authors as the anesthetic of choice.[2-5] Other writers have administered nitrous oxide[6] and ether.[7] In so far as can be determined from a study of the available literature, the employment of infiltration, nerve block, or spinal anesthetic procedures has not been advocated in the therapy of the acutely burned patient. In the reconstructive aspects of therapy for the burned patient no definite stand has been taken with regard to the choice of anesthesia by workers interested in this subject, except for the group at the Massachusetts General Hospital who cared for the patients of the Cocoanut Grove disaster.[8] In this series, twenty-one operations of a plastic nature were performed with ether as the agent of choice in thirteen, and a variety of agents and techniques for the remainder. The statement is made that no complications due to anesthesia were noted in any of the cases described.

Because of the relative paucity of information available as to the factors concerned in the proper anesthetic management of the burned patient, both in the acute and in the late or chronic stage of the injury, a summary of experience available at a large Army General Hospital appears to be in order.

CLINICAL DATA

Since the clinical material was observed at a Zone of Interior Army General Hospital, little opportunity was afforded to treat acute thermal

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burns immediately after injury. Of the patients admitted with acute burns, only six required emergency surgical intervention in the form of débridement. Two of these six were satisfactorily managed with morphine analgesia; three required pentothal sodium in very small amounts; and one, a child, was given ether by open drop technique. Since burned patients are rarely admitted to this hospital immediately after injury and are usually seen several weeks after sustaining the burn, no conclusions can be drawn based upon personal experience, but I concur in the attitude that, where possible, simple morphine analgesia is the method of choice for pain relief in the surgical management of acute burns. It should be emphasized, also, that the administration of pentothal sodium alone in the very severely burned patient is fraught with considerable danger in view of the extensive military experience in a theater of military operations,[9] where it was shown that this drug is tolerated poorly by these patients and should be avoided.

More information was obtained in the anesthetic conduct of patients in the period suitable for skin grafting and plastic surgical procedures. Twenty-seven such patients, upon whom forty-nine skin grafting procedures were performed, were admitted in a period of twenty months. The extent of the burn varied from 5 to 50 per cent of the body surface, as estimated by the section of plastic surgery in accordance with Berkow's formula.[10] In most instances, split-skin grafts were applied to the burned surfaces. The anesthetic methods consisted of spinal anesthesia for three operations in which only the lower extremities were involved in donor and recipient areas, nerve block for one procedure, ether employing carbon dioxide absorption technique in fifteen operations, and sodium pentothal (2½ per cent) supplemented with 50 per cent nitrous oxide and oxygen in thirty instances.

Premedication consisted of morphine and atropine subcutaneously approximately one hour preoperatively in cases in which pentothal was used, morphine and scopolamine in suitable doses one to one and one-half hours preoperatively for those in which ether was used, and the addition of a barbiturate to the latter for the spinal and regional anesthetics. The dosage of these drugs was somewhat less than would have ordinarily been administered because of the varying degrees of debility encountered in the patients. Earlier in the series scopolamine was given with morphine prior to the pentothal anesthesia, but the occurrence of two cases of marked laryngospasm resulting in asphyxia suggested a change to atropine as a more effective means of blocking the parasympathetic nerve endings in the larynx.[9] The more adequate prevention of laryngospasm by atropine prior to pentothal anesthesia was supported by experience in anesthesia for patients other than those in the burn group.

During the surgical procedures, a slow drip of normal saline solution was maintained to keep the intravenous needle patent at all times and

to provide a ready portal for the administration of plasma or whole blood. In general, plasma was substituted for the saline drip if operating time extended beyond one and one-half hours. If anemia was present preoperatively or if extensive bleeding occurred during operation, whole blood was administered as the fluid of choice.

In keeping with what is considered good anesthetic practice for this type of operation, the depth of anesthesia in the etherized patients was never permitted to be more profound than light second plane of surgical anesthesia. For the most part, patients were maintained in the first plane. In the patients anesthetized with the pentothal nitrous oxide sequence, the depth of anesthesia was such that at no time was respiratory activity grossly depressed. In fact, the attempt was made to maintain anesthesia only to the extent of preventing movement on the patient's part while on the operating table.

Complications attributable to anesthesia during the performance of the surgical procedures were limited in the pentothal nitrous oxide group to two cases of severe laryngospasm, requiring intratracheal intubation, described previously. This complication, it is believed, was obviated in the succeeding cases in the series by the substitution of atropine for scopolamine in the premedicant drugs administered. In the etherized patients, four of the fifteen so anesthetized in the planes described exhibited significant circulatory depression characteristic of surgical shock. With regard to the patients anesthetized with spinal or nerve block techniques, no untoward episodes were noted, but these procedures were too small in number and were of so minor a nature that the appearance of deleterious manifestations was not to be expected. It should be noted that the magnitude of surgical manipulation was similar in patients to whom ether and pentothal were administered, requiring two to five hours for the completion of operation.

In the postoperative period several observations of interest were made by way of comparison of the various anesthetics employed. There was no apparent difference in the success of viability of the graft with regard to the anesthetic employed. There was no significant change in the hematologic picture of the four patients anesthetized with spinal and regional techniques. There was a moderate depression of both red blood count and hemoglobin in the patients anesthetized with pentothal sodium, requiring an average per patient of one whole blood transfusion consisting of 500 c.c. in the immediate postoperative period. The patients anesthetized with ether exhibited a more significant anemia postoperatively, requiring on the average three blood transfusions of 500 c.c. each in a similar period of time. It should be mentioned that transfusion was given to all patients until the red blood count had reached a minimum of 3,500,000 per c.mm. with a proportionate concentration of hemoglobin. It is evident, therefore, that in patients in whom general narcosis was considered necessary for skin grafting procedures in the

treatment of burns, the pentothal sodium nitrous oxide sequence exerted a less harmful effect upon the final picture in the peripheral blood than did ether.

Some light is cast upon the present controversy concerning the concurrent use of sulfonamide drugs and barbiturate anesthesia.[11] All patients observed were given one or more drugs of the sulfonamide group preoperatively and immediately postoperatively. No demonstrable ill effects were noted in the patients anesthetized with pentothal sodium and no synergism between the two was seen. In fact, as pointed out, the course subsequent to operation in the patients anesthetized with pentothal was, on the whole, more benign than that of the etherized patients, despite the use of sulfonamide preparations. The present practice at this hospital is to utilize sulfonamide drugs, regardless of the type of anesthesia to be employed, prior to operation upon the burned patient.

There were no deaths in this series of burned patients subjected to skin grafting procedures.

DISCUSSION

In considering the choice of anesthesia for the burned patient, as has indicated, the acutely burned patient presents an entirely different problem from the patient who requires plastic surgery in the later stages of the injury. The cardinal principle of treatment for acute burns is, of course, the replacement of lost plasma by proper intravenous administration of plasma itself, or a suitable substitute. Surgical procedures should be confined to a bare minimum and the patient's condition as a whole is the important problem of therapy. For pain relief the administration of morphine is probably the least harmful and the most satisfactory method of analgesia. Where necessary, small doses of pentothal anesthesia[12] or ether anesthesia[7] may be considered acceptable but not ideal. It should be re-emphasized that the administration of any type of anesthesia producing general narcosis is not without danger in the acutely burned patient. Nerve block and infiltration techniques are useful only if the body surface burned is small in area or if the regions are supplied by accessible peripheral nerves. The employment of spinal anesthesia, particularly if the areas involved are above the tenth thoracic segment, is of considerable danger in the acutely burned patient because of the attendant circulatory depression produced by this type of anesthesia in the patient whose circulation is already impaired, either actually or potentially.[13]

In the proper anesthetic management of the burned patient in the stage of plastic repair, certain surgical requirements as well as nutritional disorders commonly seen in these patients must be borne in mind. It is desirable to maintain, in so far as possible, normal contours of the various parts concerned. This requires a reasonable maintenance of muscular tone underlying the recipient skin areas. Further, it is of

great importance in this type of surgical manipulation that a free airway be maintained to prevent capillary and venous oozing, which may result from obstructed respiration and is an important factor in decreasing viability of skin grafts. Finally, these patients very commonly suffer from anemia which requires consideration in the administration of anesthesia. Nerve block and infiltration techniques are suitable when the areas concerned in the skin grafting procedures are small enough in size to be adequately anesthetized in this fashion. If the areas concerned in the operative procedures are below the umbilicus, spinal anesthesia is considered without danger to these patients. However, as is frequently the case, either donor or recipient area will be high on the abdomen or thorax. Patients with anemia or debility do not tolerate high spinal anesthesia satisfactorily, and this technique should be avoided if the operative procedures are in the locations mentioned.

If some form of general narcosis is selected, the importance of a free airway cannot be overemphasized. If the patency of the airway cannot be assured by ordinary procedures, the employment of an intratracheal mechanical airway is indicated. This aid to respiration is necessary not infrequently and is mandatory in a position such as the prone, where ease of respiration is difficult. I am of the opinion that pentothal sodium nitrous oxide anesthesia is preferable to ether anesthesia because of the absence, in this series, of circulatory complications during anesthesia with the former, as contrasted with the latter, and the more salutary postoperative period with regard to the concentration of red blood cells and hemoglobin in the peripheral blood.

Regardless of the type of anesthesia or the drug selected, repeated emphasis is made upon the necessity for the administration of plasma or whole blood as needed during and after skin grafting procedures upon the burned patient.

SUMMARY

1. In the anesthetic management of the acutely burned patient, morphine for analgesia is the drug of choice. If morphine is inadequate, pentothal sodium or ether may be used in minimal quantities.

2. Clinical experience with various types of anesthesia in the skin grafting stage of the treatment of burns is presented. The advantages and disadvantages of the commonly employed anesthetic drugs and techniques are presented.

3. Where general narcosis is indicated for plastic surgical procedures in the management of burns, the most satisfactory results have been obtained with the employment of pentothal sodium supplemented by 50 per cent nitrous oxide in oxygen.

4. Adequate intravenous replacement therapy with plasma or whole blood, as indicated, is necessary during the operative period in the management of the burned patient.

5. The concurrent use of sulfonamide drugs and pentothal sodium exerts no clinically demonstrable ill effects.

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ORTHOPEDIC SURGERY FOR RECONSTRUCTION OF CONGENITAL MALFORMATIONS OF THE KIDNEY

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INTRODUCTION

SINCE the introduction of a systematic use of urographic examination, anomalies of the kidney have been very readily discovered. It has been found that more than 50 per cent of these anomalies were responsible for painful symptoms, which in many instances had been erroneously diagnosed and many patients had even been submitted to an unnecessary abdominal operation.

The object of this paper is to call attention to the possibility of the surgical orthopedic correction of certain congenital malformations of the kidney, by applying to surgical urologic conditions the same conservative principles that have been applied successfully in orthopedic reconstructions of other systems of the body. The idea is not a new one, yet it appears that the medical profession in general has not fully grasped the fact that malformations of the kidney are not infrequently responsible for obscure abdominal symptoms.[1] Members of the profession are apparently unaware that in such cases it is now frequently possible to relieve symptoms and effect a cure by the conservative orthopedic reconstruction of a congenitally anomalous kidney.[2]

We are living in an era in which malformations of the kidney can be diagnosed clinically before post-mortem, and in which results can be verified by the modern methods of urologic and urographic examination. The kidney and its excretory apparatus can now be visualized urographically by either one of two methods—that of excretory and that of retrograde pyelography. These methods serve to verify both the preoperative diagnosis and the postoperative results. A quarter of a century ago nothing like this could be done, and the individual who was so unfortunate as to have been born with a malformation of the kidney had to carry it unrecognized to his grave in most instances, or was subjected to operation under a mistaken diagnosis, without relief of symptoms.

The multiplicity of possible anomalies of the kidney and its excretory apparatus, and of its blood and lymphatic supply, I have classified and tabulated elsewhere, and they need not be discussed here.[1]

For purposes of this presentation, three groups of cases are to be considered, namely, those in which (1) the malformation is an accidental finding and has not produced symptoms; (2) the anomaly itself is respon-

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sible for painful symptoms; and (3) the anomaly is associated with other advanced pathologic lesions. As a rule most of the cases which come under the eye of the roentgenologist, urologist, or general surgeon are those in Groups 2 and 3, and these constitute the type of case I propose to deal with in this paper. My purpose is to illustrate the importance of making a correct diagnosis of these anomalies before operation, and to show the operative technique employed and the postoperative results obtained.

I cannot emphasize too strongly the value of conservatism in renal surgery, and the ease with which many varieties of conservative operations can be performed on an anomalous kidney, saving an organ of vital importance, which, in the past, has so often been sacrificed for lack of adequate study and proper preoperative diagnosis. These conservative principles of renal surgery have their proper application in many different types of congenital malformations of the kidney, but more especially in those involving the excretory apparatus of the organ. Among these, the most commonly observed are hydronephrosis, double kidney, horseshoe kidney, cysts of the kidney and polycystic kidney, and it is to these varieties of congenital pathologic conditions of the kidney that I shall direct my attention in this presentation.

CONGENITAL HYDRONEPHROSIS

Dilatation of the kidney pelvis for lack of drainage is caused by obstruction at the ureteropelvic junction or anywhere in the course of the ureter, and may be either congenital or acquired.

The modern clinical conception of hydronephrosis was definitely established with the introduction of pyelography, since it then became possible to visualize the kidney, to study its function more accurately, to establish a correct preoperative diagnosis, and to formulate a better prognosis. In the preurographic period most patients with hydronephrosis were submitted to the radical procedure of nephrectomy, but at the present time the tendency is to conserve as much of the renal parenchyma as possible, in an effort to save the kidney. To this end many conservative procedures have been presented from time to time which are actually plastic operations for the orthopedic reconstruction of the renal pelvis, designed to improve drainage, relieve painful symptoms, and overcome infection.[3]

Albarran[4] in 1898 was the first to introduce this orthopedic principle, by resecting the lower pole and the pelvis of a hydronephrotic kidney—an operation which was crowned with complete success. Credit for other conservative operations in preurographic days should also be given to Trendelenburg,[5] Kuster,[6] Fenger,[7] Morris,[8] Israel,[9] Bazy,[10] Terrier and Boudouin,[11] Delbert[12] and others. Thus Fenger applied the Heineke-Mikulicz procedure for pyloric stenosis to the correction of stricture at the ureteropelvic junction, a principle which has since been popularized and modified by many modern writers, among others Young,[13] von Lichtenberg,[14] Beer and Hyman,[15] Hinman,[16] Legueu,[17] Marion,[18]

Papin,[19] Foley,[20] Schwyzer,[21] Quimby,[22] Walters and Braasch,[23] Ormond,[24] Lubash,[25] Moore,[26] Gibson,[27] Priestley,[28] Mathé and De La Peña,[29] and others.

However, since the introduction of urographic studies the tendency has been to correct the hydronephrosis by removing the extrinsic or intrinsic cause of the obstruction. The most common causes of congenital hydronephrosis are: stenosis or stricture at the ureteropelvic junction with or without valve or constricted fibrous ring, aberrant polar blood vessels, fibrous bands of adhesions with kinking of the ureter, high insertion of the ureter, and malposition of the kidney. In fact all these causes may be present in the same case, but any one of them is sufficient alone to cause hydronephrosis.

The extrinsic causes are first corrected by a complete nephrolysis and ureterolysis, ligation of small aberrant blood vessels, and section of any fibrous bands of adhesion that may constrict the ureter. For correction of the intrinsic causes the three most usual plastic methods of reconstruction of the renal pelvis are: (1) section and plication of the constricted ureteropelvic junction to relieve mechanical obstruction; (2) resection of the renal pelvis with or without transplantation of the ureter to the most dependent portion of the pelvis, in order to secure good drainage; and (3) lateral anastomosis of the ureter to the renal pelvis by a Y-shaped incision, to enlarge the ureteropelvic outlet.

In the conservative treatment of congenital hydronephrosis it is of paramount importance at the close of the plastic procedure to establish proper drainage by a temporary nephrostomy. This is especially true in the infected type of hydronephrosis. The nephrostomy tube should be introduced through the cortex of the kidney into the most dependent portion of the renal pelvis. It should be accompanied by a ureteral catheter which passes on through the pelvis and into the ureter, thus serving as a splint to hold the ureter straight for the purpose of adequate drainage. This temporary drainage from the renal pelvis may also be obtained by an indwelling ureteral catheter.[30]

While the procedure of choice in congenital hydronephrosis is a conservative operation, it is obvious that if the kidney is already devoid of function the only recourse is total nephrectomy, provided of course that in the kidney of the opposite side there is a normal pyelogram and evidence of good function. In cases in which the hydronephrosis has not been satisfactorily corrected by the conservative plastic orthopedic procedure, complete relief of symptoms can still be obtained by carrying out a secondary nephrectomy.[31]

In choosing the type of conservative operative procedure for relief of uncomplicated congenital hydronephrosis, I have twice resected a polar accessory blood vessel. In three cases fibrous bands of adhesion causing kinking of the ureter were completely relieved by nephrolysis, ureterolysis, and nephropexy. In two other instances resection of the pelvis of the kidney was carried out to correct hydronephrosis, accompanied by a

temporary nephrostomy, with good success. A pyelo-ureteral anastomosis gave relief in one case of stenosis at the ureteropelvic junction; here, too, a temporary nephrostomy followed and gave good results. In another instance, where there was high implantation of the ureter, section and ligation of the ureter, followed by ureteropelvic anastomosis and temporary nephrostomy, gave complete relief. In another somewhat similar case I carried out resection of the pelvis and ureter, transplanting the latter to the most dependent part of the reconstructed pelvis in order to avoid sectioning an important aberrant blood vessel.

In all these operations for congenital hydronephrosis I have had completely satisfactory results both anatomically and functionally. I have always concluded the procedure with a nephropexy to secure a better position for the kidney and ureter, for purposes of drainage.

The good results obtained in this small series of cases have been due, first, to the careful selection of cases; second, to the use of a rigorous technique; and finally, to the fact that diversion of the urine was carried out in all cases of resection of the renal pelvis and in those of ureteropelvic anastomosis.

All these ten patients had suffered with painful abdominal symptoms over a long period of time, and in every case complete relief of these symptoms as well as of urinary disturbances was obtained.

In other types of congenital hydronephrosis with associated pathology, such as nephrolithiasis, double kidney, or horseshoe kidney, I carried out in two instances a heminephrectomy; in one case a polar resection of the kidney for stones in the upper calyx, with hydronephrosis of that calyx; and in another case the same procedure was applied successfully to a lower calyx.

In another group of hydronephrotic cases with hydro-ureters there was a combination of lesions for which I carried out a combined ureteronephrectomy or ureteroheminephrectomy, the aim in the latter case being to save the half of a double kidney by plastic operation.

Admittedly, the cases that are suitable for conservative operation must be carefully selected. It is obvious that not all cases of congenital hydronephrosis are amenable to conservative surgical procedures. Out of a group of forty cases of marked hydronephrosis that I have studied personally, in eighteen operation was not carried out; in some of the eighteen symptoms were relieved by conservative urological measures, consisting of cystoscopic treatments with dilatation of the ureters, kidney pelvis lavage, and administration of modern urinary antiseptics. However, in most of these cases, the sac of the hydronephrosis was of moderate size, was accompanied by pyelitis and pyelonephritis, and the kidney still had fairly good function as revealed by the urea estimation and phthalein elimination, as well as by urographic studies. Of the group in which operation was not done, seven cases were bilateral.

Of the remaining twenty-two patients, twelve had associated pathology or the kidney was already devoid of function, so that these necessarily

came to total nephrectomy. The other ten cases (25 per cent), therefore, represented the number found suitable for orthopedic reconstruction, by means of some form of conservative plastic procedure for correction of the hydronephrosis.

In all these cases the kidney was exposed by the lumbar route, and complete nephrolysis and ureterolysis were carried out. In some requiring drainage, nephrostomy was instituted and in most instances was maintained for from three to four or six weeks. In all cases nephropexy was performed, to place the kidney and ureter in good position for drainage. Before leaving the hospital, the anatomic and functional results were checked up in every case, in order to verify the final results obtained.

DOUBLE KIDNEY

The need for orthopedic reconstruction of a double kidney is obvious, whenever the pathologic condition in such a kidney is clearly demonstrated in the pyelogram. This is particularly true in cases in which there are persistent painful abdominal symptoms which have paved the way for erroneous diagnosis, and which have not yielded to futile abdominal operations. Whenever careful urographic studies of excretory urograms or of retrograde pyelograms have disclosed the impaired dynamism and faulty mechanics of the double kidney, as the direct cause of the delayed emptying time of the kidney, leading to intermittent crises of hydronephrosis, the malformation plainly demands appropriate surgical treatment for its correction before the complete destruction of the entire renal parenchyma takes place, which will demand total removal of the organ.

In carefully selected cases of double kidney with painful symptoms it appears that some type of conservative operation should be carried out to reconstruct the anomalous organ, thereby providing it with normal function. Here too, as in hydronephrosis, there are several types of plastic procedure which are capable of achieving this end. Among these are (1) anastomosis of the two renal pelves; (2) anastomosis of the upper ureter to the lower renal pelvis; (3) anastomosis of the two ureters at any level; (4) transplantation and reimplantation of one or both ureters; (5) anastomosis of the lower renal pelvis to the bladder in certain cases of ectopic double kidney, and (6) heminephrectomy, or resection of one-half of the double kidney, with or without removal of the corresponding ureter.

Anastomosis of the two renal pelves or of the two ureters has seldom achieved permanent cure, and most of the cases in which it has been employed have unfortunately come sooner or later to secondary nephrectomy. When one is confronted, therefore, with a case of double kidney and double ureter in which an unavailing abdominal operation has been performed, without relief of symptoms, the best prospect of cure lies in carrying out a heminephrectomy.[32]

I had the opportunity not so long ago to operate upon a patient with a case of this kind with gratifying results. She was a young woman who had been operated upon elsewhere for chronic appendicitis, but symptoms were not relieved. Upon urographic examination she was found to have an enlarged right double kidney with double renal pelves and ureters. The ureters, after crossing one another, became united above the bladder, resulting in urinary stasis, with marked dilatation at their point of union, as well as pyelectasis and caliectasis. Pyelitis and pyelonephritis were present, along with an appreciable degree of nephroptosis. When medical treatment failed to bring relief, the patient was completely cured by resection of the upper pole of the double kidney and removal of the corresponding ureter, followed by nephropexy of the half of the kidney left in situ, with a view to straightening the ureter and securing good drainage. Three weeks after operation the pyelogram revealed a normally functioning right kidney, thus confirming the success of the orthopedic procedure. The patient has since given birth to a baby without any urinary inconvenience, and is now completely free from symptoms.

Owing to the almost inevitable faulty mechanics of a double kidney, resulting in dynamic dysfunction of the excretory apparatus of the kidney, the emptying time is retarded and the elimination incomplete in one or both pelves of the double organ. This is plainly shown in the delayed urogram taken one or more hours after intravenous injection of the opaque substance, demonstrating the actual surgical pathology present in the double organ.

As the crossing of the two ureters in the double kidney is quite characteristic in this malformation, interfering with the physiologic peristaltic contraction and retarding the emptying time of the renal pelves, we have here essentially the same phenomenon of an extrinsic mechanical factor that we commonly observe in cases of aberrant blood vessels, causing obstruction at the ureteropelvic junction, and resulting here too in hydronephrosis.

For the same reason, therefore, that we remove an aberrant blood vessel for the orthopedic surgical relief of hydronephrosis in a single kidney, we likewise in double kidney do a heminephrectomy with removal of the corresponding ureter, in order to relieve mechanical obstruction and achieve a permanent cure, with complete disappearance of symptoms, whether abdominal or urinary.

HORSESHOE KIDNEY

Among the most important congenital malformations of the kidney, demanding operative intervention, with orthopedic surgical reconstruction of the anomalous organ to relieve painful symptoms, is the classic horseshoe kidney.[33]

In the surgical treatment of horseshoe kidney I have elsewhere described four groups of cases which we can now reclassify for practical purposes into five groups as follows:

Group 1. Silent horseshoe kidney without any painful symptoms.

Group 2. Horseshoe kidney associated with indefinite abdominal pain, urinary symptoms and gastrointestinal disturbances.

Group 3. Horseshoe kidney associated with gross pathologic lesions in one-half of the fused organ.

Group 4. Horseshoe kidney associated with gross pathologic lesions in both renal pelves.

Group 5. Horseshoe kidney associated with other types of anomalies, such as the presence of three or four renal pelves and ureters.

We are here concerned with the most common type, the cases usually observed clinically, such as those listed in Groups 2 and 3, which demand some form of surgical orthopedic reconstruction to relieve symptoms and bring about a permanent cure.

Although operations for reconstruction of fused kidneys were performed previous to the urographic era, it is only rather recently that they have become popularized. In the past most of the operations performed on the horseshoe kidney were done, not for the anomaly per se, but for the relief of associated pathology in one-half of the double organ, for which such procedures as heminephrectomy, nephrolithotomy, pyelolithotomy, or even ureteropelvic anastomosis has been carried out.

For the orthopedic reconstruction of the anomaly per se, however, in order expressly to relieve painful symptoms for which it alone is responsible, no procedures have been envisaged until rather recently, when Papin,[34] Foley,[35] Gutierrez,[2] and others advocated symphysiotomy or division of the renal isthmus as a means of relieving persistent symptoms and providing a definitive cure.

In a typical case in which I recently operated successfully upon the patient, a woman had been suffering for long years with what I have called the horseshoe syndrome, or the horseshoe kidney disease, consisting of indefinite abdominal pain, urinary symptoms and gastrointestinal disturbances. After she had received treatment for chronic cholecystitis, chronic appendicitis, colitis, and other abdominal complaints for many years, to the extreme of becoming practically a neurotic for lack of relief of her symptoms, her condition was finally diagnosed as horseshoe kidney, for which she was referred to me for examination and treatment. The complete urologic and urographic examination disclosed the presence of a horseshoe kidney with pyelitis and pyelonephritis, marked urinary stasis, and evidence of pyelectasis and calyectasis, thus clearly revealing that the patient was suffering with the horseshoe kidney disease.

In this case, after proper preliminary preparation, I carried out an orthopedic reconstruction of the fused organ by an extraperitoneal

symphysiotomy operation, or division of the renal isthmus, followed by nephrolysis, ureterolysis, and right nephropexy.[2]

The purpose of this orthopedic procedure was, first, to relieve the pressure of the isthmus upon the great abdominal vessels by separating the two kidneys from each other and rotating them outward from their midline position to occupy their normal position, one in each lumbar region, and second, to relieve the mechanical obstruction of the ureters, caused by their ventral position in front of the renal isthmus, which interferes with good drainage.

The postoperative results of this plastic procedure for division of the renal isthmus were truly dramatic. Three weeks after the operation the retrograde pyelograms and the renal functional tests revealed not only that both kidneys were working perfectly and appeared to be in their normal position, but also that the ureters likewise had assumed the correct position and were providing good drainage. The operation for the orthopedic reconstruction of the anomalous organ was thus entirely satisfactory, and the patient was relieved of all symptoms, abdominal and gastrointestinal as well as urinary.

From this case it is possible to see the necessity of recognizing in advance the indications for applying the principles of orthopedic surgical reconstruction in cases of horseshoe kidney associated with the horseshoe kidney syndrome.

In addition to symphysiotomy for division of the renal isthmus, even a symphysiectomy can safely be carried out, if indicated, removing the entire isthmus of the horseshoe organ, as in a case recently reported by Lower,[36] when a nephrectomy was successfully performed for removal of a third kidney ensconced in the middle portion of the isthmus of the horseshoe organ.

For cases of horseshoe kidney included in Group 3, in which the anomalous fused organ is accompanied by some gross type of pathologic lesion in one of its halves, several forms of surgical procedure are available. Among the simpler are pyelotomy and nephrotomy for removal of stones, and nephrostomy to provide drainage in pyonephrosis. Among the orthopedic procedures are pelvi-ureteral anastomosis for correction of hydronephrosis, and heminephrectomy for removal of one-half of the horseshoe organ in cases of advanced nephrolithiasis, tuberculosis, or tumor, and also in cases in which one of the halves is devoid of function.

Horseshoe kidney associated with bilateral nephrolithiasis can also be submitted to orthopedic correction, the type of surgical procedure being chosen on the basis of the functional capacity of the respective kidneys that constitute the fused organ. The procedure should be carried out first on the better side, so that, if it becomes necessary, heminephrectomy can be carried out in the kidney of the opposite side.

CONGENITAL CYSTS OF THE KIDNEY

Two distinct types of congenital cysts of the kidney confront the surgeon, namely the large solitary cysts of the kidney and the poly-

cystic kidney. I have presented elsewhere a classification of the many different varieties of cysts of the kidney in a report on ten cases, delivered before the American Urological Association in 1941.[37] I have also described the operative technique employed in the orthopedic correction of this cystic type of malformation by suitable resection, and the results obtained thereby.

Both of the two principal types of cystic malformations of the kidney were formerly regarded exclusively as medical entities, and were in fact seldom correctly diagnosed preoperatively. With the advent, however, of the modern means of diagnosis, accuracy in the differentiation of these two entities is now possible, and their orthopedic surgical correction has been made feasible in some cases.

Although this cystic condition is congenital, it is not often recognized until painful abdominal symptoms make their appearance, or until urinary disturbances call for a complete urographic and urologic examination. Large solitary cyst of the kidney is as a rule unilateral, while polycystic kidney is generally bilateral. Both conditions are today, to a certain extent, amenable to conservative surgical correction.

Large Solitary Cyst of the Kidney.—The large solitary cyst of the kidney may be located in any part of the organ. When it is in the upper pole of the right kidney it may easily be mistaken for some other pathologic lesion of the right upper quadrant of the abdomen, and its diagnosis is then difficult unless it is clearly visualized roentgenographically. The renal symptoms may in fact be completely masked by those of the liver and gall bladder, upon which the cyst impinges; hence, these cysts frequently give rise to gastrointestinal manifestations.

These large serous cysts fall anatomicopathologically into two groups: (1) cysts connected with a calyx or the renal pelvis, and (2) cysts that have no such connection. The latter are far more common, and may exist for many years without giving symptoms until they reach an enormous size, sometimes becoming several times the size of the kidney itself. According to the type of their content these renal cysts may be classified as serous, hemorrhagic, purulent, tumor containing, calcified, hydatid, dermoid, or tuberculous. The renal cyst may also be accompanied by hydronephrosis or other type of pathologic condition of the kidney, such as stone, or cancer. Although usually unilateral, the cyst may be found in both kidneys and occupying both poles. In the most common type, however, it is located in the upper or lower pole of one kidney. A cyst may remain silent until its pressure upon surrounding structures results in painful symptoms, chiefly abdominal. As soon as infection sets in, it also causes hematuria and pyuria, giving evidence of pyelitis and pyelonephritis.

The modern tendency in conservative renal surgery is to resect the cyst in order to save the kidney. The procedure will vary with the individual type of case. Obviously when the kidney parenchyma has been

destroyed by compression of the cyst, and the kidney has become functionless, nephrectomy must be carried out. But when the cyst has involved only a limited portion of the parenchyma, a conservative orthopedic operation can still be performed to relieve the organ of its malformation and its painful symptoms. This will consist of removing the cyst and carrying out a complete nephrolysis, ureterolysis, and nephropexy. When the cyst is very large and has destroyed a considerable amount of renal parenchyma, an orthopedic resection of the entire upper or lower pole is called for. When it is connected with a calyx, partial resection including a calycectomy should be carried out, after which the calyx should be sutured to prevent leakage of urine, and the raw surface of the kidney covered with fat to prevent bleeding. Care should of course be taken to see that the blood supply of the remaining portion of the kidney is adequate.

Experience has shown, therefore, that the kidney upon which a large solitary cyst has developed can, in the majority of cases, be definitely corrected by a conservative orthopedic procedure, consisting either of a total resection of the cyst alone, without parenchyma, or of a partial nephrectomy, designed to reconstruct the anomalous organ, to relieve symptoms, and to restore function.

Polycystic Kidney.—Polycystic disease of the kidney is a congenital malformation of the kidney, characterized by formation of multiple cysts of the renal parenchyma. It is generally bilateral and progressive, with a tendency gradually to destroy the kidney parenchyma, diminish renal function, and hasten renal failure. It is quite commonly found in association with surgical pathologic conditions and, in most instances, with pyelitis and pyelonephritis, causing hypertension, and gastrointestinal disorders. In advanced cases the polycystic kidney may be enormously enlarged and may occupy the entire flank on each side of the abdomen. The diagnosis can be definitely made with complete urographic studies, in which the pyelogram will disclose the typical elongation of the calyces, thus serving to confirm the polycystic condition.

The clinical importance of recognizing this entity lies in the fact that whereas in the past polycystic kidney was considered exclusively a medical entity, we know today that the condition can in reality be corrected to some extent by conservative surgery, and the symptoms relieved, thus prolonging life and providing comfort.

Three types of cases must be considered: (1) The polycystic disease is still silent, and gives no symptoms. (2) There are present not only painful abdominal symptoms but also urinary disturbances, the gastroenterorenal syndrome, uremic symptoms, and hypertension. (3) In addition to the symptoms in Group 2, there is also a concomitant pathologic lesion, such as hydronephrosis, stones, tuberculosis, tumor, rupture of a cyst with hemorrhage, or infection of a cyst. All of the cases that give rise to painful symptoms are amenable to relief by conservative surgical measures.

With accuracy in diagnosis and proper preliminary preparation, many of these patients can be operated on successfully today, not only to correct in some degree the congenital malformation, but also to relieve symptoms and prolong what may be a life of comfort by carrying out some type of orthopedic procedure which will restore better function.

Many conservative surgical procedures have been employed for relief of this congenital malformation of the kidney, such as aspiration of cysts, multiple puncture of cysts, renal decapsulation, and resection of cysts. Goldstein[38] recently described a method of anchoring the kidney to the skin, after a partial cortical nephrotomy to create a nephrocutaneous fistula, thus facilitating a repetition of the aspirations as often as necessary to relieve the tension of the cysts. Other types of conservative operation, such as nephrolithotomy, pyelolithotomy, and nephrostomy, have also been carried out. Even nephrectomy can be performed, provided there is sufficient function in the kidney of the opposite side.

I have operated successfully upon five patients (my own cases) with polycystic kidney and associated pathology, performing two nephrectomies, one of which was for tumor and the other for persistent bleeding; one with pyelolithotomy, and one with nephrolithotomy; and in one interesting case I operated upon both kidneys for relief of an infected polycystic condition, carrying out a multiple aspiration of cysts and bilateral renal decapsulation.[39]

In this last case the patient was suffering with advanced uremic symptoms, paralytic ileus, and marked hypertension. The excretory and retrograde pyelographic studies revealed that the left kidney was obviously polycystic in character and of enormous size, occupying the entire left abdomen. The right kidney was practically functionless and the retrograde studies disclosed an atrophic type of polycystic kidney. I operated upon the left kidney first, aspirating multiple small cysts and in addition two large ones containing, respectively, 40 c.c. and 50 c.c. of pus. I then decapsulated the kidney, to which the extraordinarily thick capsule was closely adherent. Six weeks later I operated on the right kidney, aspirating multiple small and large cysts and decapsulating this kidney also. The results were excellent in both operations. The postoperative checkup showed that both kidneys had gained in function and that the patient was entirely free from symptoms.

SUMMARY AND CONCLUSIONS

1. Every anomaly of the kidney is a potential surgical condition.

2. Congenital malformations of the kidney giving symptoms are frequently amenable to surgical orthopedic correction by plastic surgery.

3. Anomalies of the kidney are often responsible for painful abdominal symptoms.

4. Many futile abdominal operations have been performed for symptoms referable to an unsuspected renal anomaly

5. Among the most common unrecognized anomalies of the kidney are congenital hydronephrosis, double kidney, horseshoe kidney, large solitary cyst of the kidney, and polycystic kidney, which are here discussed in detail.

6. Many congenital malformations of the kidney demand conservative surgical intervention to relieve symptoms that are due to the anomaly per se.

7. Orthopedic surgical reconstruction of the malformed kidney has found its definite place in modern urology.

8. When excretory urographic studies reveal the presence of a congenital malformation, the patient should be submitted to a complete urologic examination, including bilateral retrograde pyelograms.

9. Plastic surgery for the correction of renal anomalies should be carried out only in well-selected cases, since it is obviously useless in a kidney already devoid of function.

10. Every patient submitted to orthopedic surgical reconstruction of an anomalous kidney should be checked functionally and urographically before leaving the hospital, in order to ascertain the results obtained.

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EXTENSIVE VARICOSITIES OF THE LEG ORIGINATING FROM THE GLUTEAL VEIN

Report of a Case

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(From the Department of Surgery, Medical College of the State of South Carolina)

THE case herewith reported is of interest because the very extensive varicosities of the right leg originated from the inferior gluteal vein. This vein is a tributary of the internal iliac, whereas the saphenous vein, which is involved in almost all cases of varicosities of the legs, is a

Fig. 1.—Photograph taken Feb. 9, 1940.

tributary of the external iliac through the femoral. In a review of the recent literature there was found no mention of varicosities of gluteal origin. The history of this case strongly indicates that the condition was of developmental origin.

Received for publication, July 3, 1944.

CASE REPORT

CASE 1 (REPORT NO. 31936).—O. B., a 37-year-old white man working as a carpenter, was admitted to the Riverside Infirmary Feb. 9, 1940. He had been aware of large veins in the right leg since childhood. He recalled having had, at the age of 10 to 12 years, ulcers which were slow in healing. For many years he had worn tightly laced knee boots constantly in order to support the leg. His general health had been good. He was well developed and well nourished. Examination revealed no finding

Fig. 2.—Feb. 9, 1940, point pressure over inferior gluteal vein after emptying veins by elevating the leg.

of note other than that pertaining to the right leg. Fig. 1 adequately portrays the extensive varicose veins on the posterolateral aspect of the thigh and the lower leg. There was no appreciable involvement on the medial aspect, however the great saphenous vein was readily palpable in the lower thigh. The varicosities were easily emptied by elevating the leg (Fig. 2). When empty, point pressure applied over a large vein in the lower gluteal region prevented their rapid filling upon the patient's standing. Release of the pressure resulted in rapid filling from above downward. A diagnosis was made of varicose veins originating from the inferior gluteal vein.

Feb. 10, 1940, operation was performed under nitrous oxide anesthesia. An incision was made over the large bulbous varicosity in the inferior gluteal region. The vein was isolated, severed, and its upper segment dissected to its point of disap-

pearance into the gluteal muscle. An attempt at stripping the distal segment met with failure due to its thin wall and adherence to the skin. A ureteral catheter was passed into it downward for two-thirds the length of the thigh, and 10 c.c. of 5 per cent sodium morrhuate were injected during the withdrawal. The ends of the vein were ligated with plain catgut and the skin edges approximated with clips. A moderately large vein situated several centimeters anterior and inferior to the main trunk was isolated by dissection, severed, and its ends ligated. An elastoplast bandage was placed from the toes to the knee. Considerable phlebothrombosis followed this procedure, however there was no general swelling of the leg. During the next few

Fig. 3.—April 3, 1941, after treatment.

months, at intervals of one to several weeks, some of the remaining patent varicosities were injected with sodium morrhuate. The patient was last examined Feb. 2, 1943. He had been working steadily. There was no swelling of the right leg or foot, and he complained of no symptoms. There were several moderate-sized varicosities on the lateral aspect of the lower leg.

A NEW HEMOSTATIC CLAMP

Description of a Hemostat Carrying Multiple Preformed Ligatures

Gonzalo Cubero O., M.D., San José, Costa Rica

SINCE the control of hemorrhage is essential in any operation, any procedure which will facilitate it is worth while. In the present communication is described an ingenious new hemostatic clamp, which through a particular modification can hold one or more ligatures with a special knot, which will be described, already prepared so that they can be tied at the same time that the clamp grasps the bleeding vessel. With this instrument one is enabled to place rapidly and consecutively one or more ligatures without the necessity of an additional maneuver except for the clamping of the bleeding vessel and the necessary traction on the suture ends to fix it.

The clamp resembles a péan forceps (Fig. 1). The lower arm has practically no modification; the upper arm is curved between the joint and the grasping end with dentations on its undersurface; and there extends distally from the region of the joint an additional short arm, which has the form of a half-cylinder that serves to hold the loop of the ligatures. On the opposite end situated above the thumb grasp is a transverse bar constructed like an automobile spring between the leaves of which the free ends of the ligatures are wedged in alternate succession. This provides immediate access to the ends, which can be freed separately and readily by the assistant who simply detaches them and closes the knot while the operator releases the clamp from the grasped vessel. The clamp can be loaded under aseptic conditions by the suture nurse prior to the operation. Consequently, one may have any number of previously prepared ligatures in triplicate amount depending upon the number of clamps so prepared and needed.

Knot.—The knot is an old one which is frequently used except in medicine. It is the double-hitch knot (Fig. 2) and consists of two loops made clockwise (Fig. 3) with the second placed back of the first (Figs. 4, 5, and 6).

Technique of Usage.—Following the incision the operator takes one of these clamps and seizes the bleeding vessels while his assistant by detaching the free ends of the ligature from the special holder simply exerts traction, thereby closing the loop and securing the vessel, the loop being automatically detached from its tilelike ridge by this maneuver. The nature of this loop is such that when it is drawn taut about the vessel it fixes it in such a manner that it cannot slip, and the application of a second knot is unnecessary. Subsequently, all that is necessary is to sever the free ends above the knot. In this manner, by use of the same instrument, the surgeon simply repeats the instrument application and is able to ligate three bleeding points in rapid succession.

Received for publication, June 13, 1944.

Advantages.—The advantages of this clamp are:

1. It reduces the operating time considerably and prevents fatigue on the part of the surgeon.

2. The double loop provides a ligature which is much stronger than the average tie.

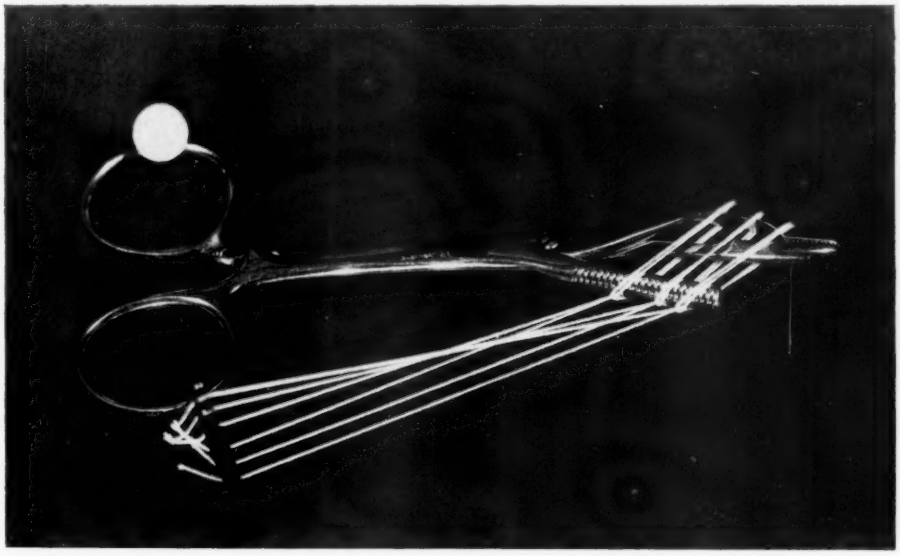


Fig. 1.—Photograph of the hemostatic clamp loaded with three ligatures. The upper arm (lower jaw) is curved between the joint and the grasping end and has dentations on its upper surface. Extending distally from the region of the joint on the upper arm is an additional short arm, which has the form of a half-cylinder which serves to hold the loop of ligatures.

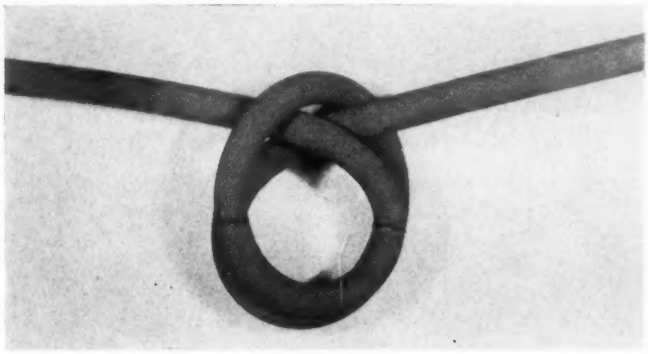


Fig. 2.—Double-hitch knot which is used for the ligatures.

3. The surgeon may concentrate his observation and vision upon the detail of clamping the vessel and is not distracted from the operative field by having alternately to grasp a vessel and then apply a ligature. In a like manner the assistant devotes his attention simply to securing the knot and cutting the free ends, thus obviating at least two manual procedures which are necessary in the conventional application of clamp and ligature.

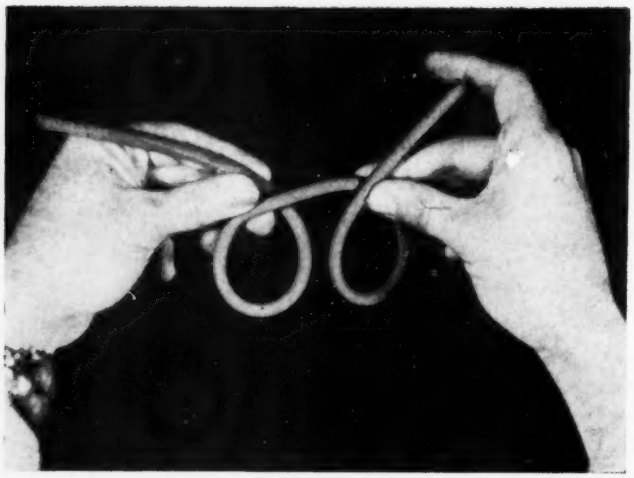


Fig. 3.—The first step in the making of the double-hitch knot. A clockwise loop is made and held in the left hand; another clockwise loop is made and held in the right hand.

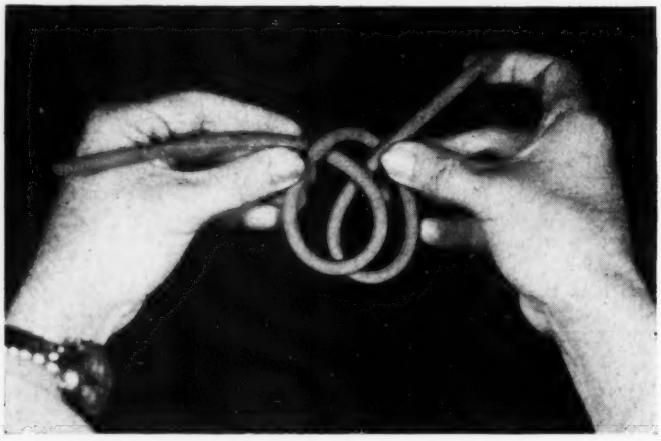


Fig. 4.—Two loops are placed together, placing the second loop back of the first.

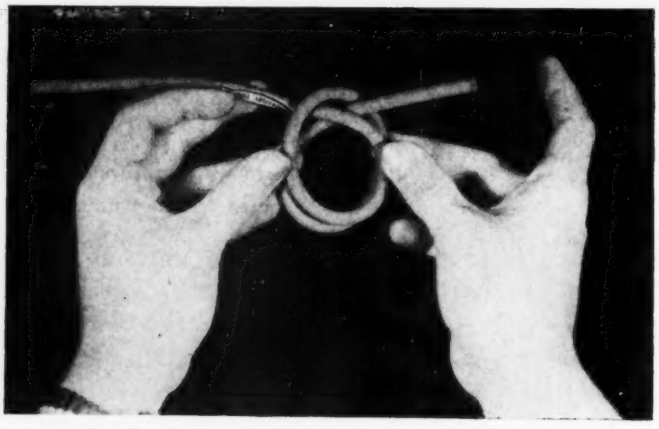


Fig. 5.—The completed double-hitch knot.

4. Since the loop is previously prepared, no knot has to be tied, which is always time-consuming and at times difficult because of the tendency of the ligatures to adhere to the wet gloved fingers.

5. *On the battle front or in emergency stations or outpatient clinics* where no physician is available immediately, any attendant may control bleeding vessels rapidly by means of this clamp, which has been loaded

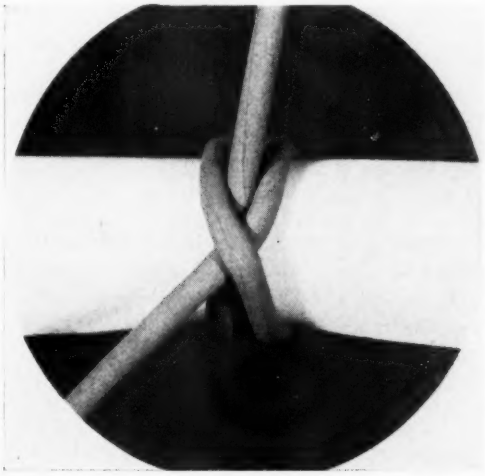


Fig. 6.—The double-hitch knot viewed from above showing the manner in which the knot is held.

previously and sterilized and kept under aseptic conditions, without the necessity even of washing his hands since the loop can be applied without contamination.

6. The loop can be made easily by performing two loops in a clockwise manner, the second loop being placed behind the first.

7. A long-handle model mounting a single loop is invaluable in the ligation of bleeding vessels which must be grasped through a small aperture and secured at a great depth.

Review of Recent Meetings

FIFTY-SECOND ANNUAL MEETING OF THE WESTERN SURGICAL ASSOCIATION

CHICAGO, ILL., DEC. 1 AND 2, 1944

HERBERT H. DAVIS, M.D., OMAHA, NEBR.

1. **Madura Foot, Francis E. Clough,** San Bernardino, Calif.—Madura foot disease does not occur just in the tropics. Forty-eight cases have been reported in the United States. There is no specific treatment. Amputation is often necessary.

2. **The Technic for Closure of the Ring of Post-Operative Abdominal Hernia, Neil J. Maclean,** Winnipeg, Man., Canada.—In the upper abdomen the strong lateral pull of the abdominal muscles causes the hernia ring to have the long diameter transversely, therefore, closure should be done transversely. In the lower abdomen, however, the long diameter is usually vertical, therefore, the closure should be vertical. For the closure of the umbilical hernia Dr. Maclean advised the three-flap method.

3. **Interscapulo-Thoracic Disarticulation of the Arm,** Jacob K. Berman, Indianapolis, Ind.—Disarticulation of the arm is being revived. Main indications are malignant tumors, sarcoma of bone, carcinoma with axillary metastases, and, occasionally, cases of severe trauma. The technique of the operation was described.

4. **Postoperative Deaths, Erwin R. Schmidt** and (by invitation) **Ralph M. Waters and Noel Gillespie,** Madison, Wis.—This report was based on the records of deaths in 56,000 cases. Deaths on the operating table were due to cardiac conditions, hemorrhage, or anesthesia. Those in the first twenty-four hours following operation were mainly circulatory or central nervous system failures. Those deaths occurring later were mainly due to infection and emboli.

5. **The Use of Thiouracil in the Treatment of Hyperthyroidism, Arnold S. Jackson,** Madison, Wis.—A study of thirty cases was reported. Indications were: iodine-resistant cases, advanced toxic adenoma, adenoma with complications, severe exophthalmic goiter in very young, very old, or debilitated patients, exophthalmic goiter with pregnancy or other diseases, iodine-fast hyperthyroidism, and recurrent or persistent hyperthyroidism. No definite conclusions were given; however, the opinion was expressed that use of thiouracil would not supplement surgery in exophthalmic goiter, but that it will be a valuable adjunct in the treatment of primary or secondary hyperthyroidism.

From the literature Jackson reported that at least seven cases of fatal agranulocytosis have occurred following its use.

6. **Thyroidectomy by the Off the Trachea Method, Martin C. Lindem,** Salt Lake City, Utah.—Lindem advised removing the thyroid by first cutting through the isthmus, then dissecting the lobe from the trachea. In this procedure he feels that there is less danger of injuring the recurrent laryngeal nerves, or the parathyroids, and that much better exposure of the superior thyroid poles can be obtained.

Received for publication, Dec. 23, 1944.

7. **Amino Acids Used Intravenously in Surgical Patients, Herbert H. Davis,** Omaha, Nebr.—The importance of giving protein following operation was stressed. The results of giving intravenous protein digest to 203 surgical patients were given, showing, clinically, a very much improved general condition. There were no serious reactions. Minor reactions occurred in 3 per cent of the injections.

8. **The Use of Skin Flaps in the Repair of Scarred or Ulcerative Defects Over Bone and Tendons, Earl C. Padgett** and (by invitation) **John H. Gaskins,** Kansas City, Mo.—Ninety-seven cases were reported with the use of skin grafts. They are for the repair of defects over bones and tendons.

9. **The Origin and Growth of an Adenoma of the Islands of Langerhans, Louis P. Good,** Texarkana, Texas.—In a very thorough histopathologic study it was concluded that an adenoma of the islands of Langerhans arises as a result of proliferation of the duct epithelium.

10. **Resection of Pancreas for Hyperinsulinism, Stanley R. Maxeiner,** Minneapolis, Minn., and (by invitation) **Colonel Harry E. Bundy.**—A case was reported of a discharged soldier, aged 24 years, with typical symptoms, blood sugar going as low as 28 mg. per 100 c.c. At operation 75 per cent of pancreas was removed. There were eight islet tumors. Since the operation the symptoms have been relieved; the blood sugar is stabilized near 100 mg. per 100 c.c.

11. **Resection of the Duodenum and Head of the Pancreas for Carcinoma, Warren H. Cole** and (by invitation) **John Reynolds,** Chicago, Ill.—Five cases were reported, with one death. One of the four patients still has a pancreatic fistula, and the other three are in good condition. These authors use long loop jejunum, anticipating that they may, at some time, anastomose the pancreas to the jejunum, and place a drain to the region of the pancreas. None of the patients had ascending cholangitis. They feel that the danger of this is lessened by anastomosing the common duct to the jejunum, rather than anastomosing the gall bladder, and that the anastomosis should be made proximal to the anastomosis between the stomach and the jejunum so that the stomach content does not flow over the area.

12. **Pancreaticoduodenectomy for Carcinoma of the Ampulla, Thomas G. Orr,** Kansas City, Kan.—There have been 105 cases of pancreaticoduodenectomy previously reported, including nine cases which Orr reported. Great care should be taken to be sure that the diagnosis is carcinoma. If in doubt, open the duodenum and get biopsy.

The choice of whether to do this procedure in one or two stages should depend upon the condition of the patient. In selecting a technique, one should be adopted which can be done in the shortest time. Enough tissue should be removed and the bile duct used rather than the gall bladder in making anastomosis. Orr believes in restoring the physiology of digestion, by anastomosing the pancreas to the bowel.

13. **Gastric Resection for Certain Acute Perforated Lesions of the Stomach and Duodenum With Diffuse Soiling of the Peritoneal Cavity, J. Dewey Bisgard,** Omaha, Nebr.—Six cases of perforation of the stomach with soiling of the peritoneal cavity were reported in which a gastric resection was done without a fatality. They were all done on men varying from 26 to 62 years of age. Two operations were for carcinoma and four were for ulcers. One of the patients with carcinoma lived twenty months, and the other, three months following operation, dying later from the carcinoma. The four patients with benign ulcer are alive and in good condition.

14. **Surgical Treatment of Pharyngo (Esophageal) Diverticulum Review of 140 Cases, Stuart W. Harrington,** Rochester, Minn.—So-called esophageal diverticula really originate in the hypopharynx. A discussion of the one- and two-stage excision of the diverticulum was given, and relative merits evaluated. Harrington favors one-stage operation. He reported 140 cases, 25 of whom were treated by the two-stage operation, with 1 death, and 115 with one-stage operation, in which there were no deaths.

15. **A Review of One Hundred Subtotal Gastrectomies for Benign Ulcers, Robert L. Sanders,** Memphis, Tenn.—It was pointed out that there was a changing attitude favoring earlier surgical approach to gastric ulcers. In Sanders' series, 22 per cent of the gastric ulcers were carcinoma. He stated that even carcinoma will partially heal over for a short time with medical treatment. In high resections he does an anticolic anastomosis. Routinely, he removes 55 to 60 per cent of the stomach. He stated that there is likely to be nutritional disturbances if more is removed. Since 1940 he has not done a single pyloroplasty. The operative mortality was 3 per cent. When the duodenal ulcer is firmly adherent to the pancreas, he cuts the duodenum across proximal to this, and inserts his finger in the open end as a guide in the dissection.

16. **Gastro-Jejuno-Colic Fistula, Henry K. Ransom,** Ann Arbor, Mich.—The treatment for fistula is necessarily surgical, but the poor condition of the patient and the severe inflammatory reaction about the lesion has been responsible for a high mortality rate. During the years 1934 to 1944, at the University of Michigan Hospital, forty-seven patients with jejunal ulcers were operated upon. Of these, eight had gastro-jejuno-colic fistulas. Ages varied from 31 to 72, the average being 49 years. All but one of the patients were men. The original operation was always a posterior gastroenterostomy.

Two different types of operation were used: I. Radical with gastric resection; II. conservative without radical resection, restoration of the bowel with a typical closure. Fourteen operations were done with two deaths, or 14.3 per cent mortality. One of the deaths was due to a leak resulting in peritonitis, the other to empyema from rupture of a lung abscess.

17. **Surgical Management of Sigmoidal Carcinoma Involving the Urinary Bladder. Review of Sixty-Four Cases, Claude E. Dixon** and (by invitation) **Raymond E. Benson,** Rochester, Minn.—Sixty-four cases were reported, 40 patients with extensive resections, and twenty-four with metastases; resection was not done. In the forty resections there were seven deaths. It is advisable to treat these lesions radically, as they often do not metastasize early. The operation consists of removal of part of the bladder with the tumor and an end-to-end anastomosis of the colon.

18. **Preservation of the Sphincters and Intestinal Continuity in Operation for Carcinoma of the Rectal Ampulla, Owen H. Wangensteen,** Minneapolis, Minn.—Resection with primary anastomosis, and without an external decompressive vent, is done routinely in Wangensteen's clinic for all unobstructed lesions of the colon demanding partial excision. Carcinoma of the rectosigmoid juncture is treated in the same manner. Such procedures can be accomplished with low risk. In suitable instances of carcinoma of the rectal ampulla, the lesion lying 5 cm. or more above the pectinate line, it is possible to preserve the sphincters and effect a satisfactory removal of the segment of the rectum involved with its lymphatic drainage area. A small perineal incision is made for drainage. Function is usually good.

19. **Peripheral Nerve Injury in Association With Fractures of Long Bones, Charles G. Johnston** and (by invitation) **E. S. Gurdjian,** Detroit, Mich.—A series

of sixty-five operated cases of nerve injury in association with fractures of long bones is analyzed. He discussed advisability of neurolysis for the excision of a neuroma with end to end suture of the nerve.

20. **Repair of Peripheral Nerves in the Presence of Extensive Soft Tissue and Bone Injuries of the Extremities, Loyal Davis** and (by invitation) **George Perret** and **Walter Carroll,** Chicago, Ill.—If there is a contamination the authors advise introducing sulfathiazole jelly into the depth of the wound at the time of operation. In case of loss of nerve substance where the nerves cannot be brought together, the use of grafts has a definite place. Autogenous grafts of the same size are best. Later it is often necessary to resection and resuture the distal ends as the nerve fibers cannot get through the scar. Nerve graft banks are in the process of development. Cable grafts are not advised. If autogenous grafts are not available, fresh homogenous grafts may be used.

In severe injuries of nerves, the reaction to the injury may extend both ways in the nerve, proximally as well as distally, therefore, it is often necessary to resect the portion of the nerve proximal to the injury. This point has often been neglected.

21. **Chronic Sclerosing Osteitis: Differential Diagnosis, Henry W. Meyerding,** Rochester, Minn.—Meyerding reviewed a series of cases seen at the Mayo Clinic in a period of thirty-two years from 1912 to 1943, inclusive. He discussed the symptoms, differential diagnosis, and treatment, which is surgical excision. The results were excellent.

22. **The Treatment of Infected Pin Operations for Fracture of the Neck of the Femur, Kellogg Speed,** Chicago, Ill.—Onset is usually insidious and not alarming. Attempts at renailing may unhappily be made; usually the fixation agent is finally withdrawn and little else is done. The patient drifts into a condition of chronic osteomyelitis with bed confinement, discharging sinuses, dislocation of the hip, loss of weight, and strength, and may die from the effects or general sepsis. The ilium and acetabulum may become infected and necrotic.

Treatment consists in early recognition, prompt, adequate drainage, and fixation in plaster. Sulfonamide drugs and penicillin may be used if applied wisely. When the head of the femur dies its removal is imperative before the condition can be overcome.

23. **Status of the Bone Graft in Ununited Fractures of the Neck of the Femur, Melvin S. Henderson,** Rochester, Minn.—In a certain percentage of cases, unfortunately not high, the bone graft can be used. The fibula may be used as a peg, without exposing the joint, by drilling a channel through the trochanter and neck, well into the head. A guide wire and a special drill are used. Results were excellent in twelve of fifteen cases, that is in 88 per cent. A double spica cast is applied. The patient is kept quiet from one to three months.

24. **Personal Evaluation of Vitallium Cup Arthoplasty of the Hip Joint, Glen Evan Cheley,** Denver, Colo.—Cheley had this operation performed upon himself. He discussed the course of the disease, and his pre- and postoperative treatment and results.

Notices

BARUCH COMMITTEE ON PHYSICAL MEDICINE

The Administrative Board of the Baruch Committee on Physical Medicine has announced the granting of an additional total sum of $185,000, which is being given by Mr. Bernard M. Baruch for the further advancement of the program in physical medicine and the physical rehabilitation of those disabled in the war. This sum has been divided into seven grants as follows: $50,000 to the Massachusetts Institute of Technology, Cambridge, Mass.; $40,000 to the Medical School of the University of Minnesota, Minneapolis, Minn.; $30,000 to the Medical School of Harvard University, Boston, Mass.; $30,000 to the Medical School of the University of Southern California, Los Angeles, Calif.; $15,000 to the Medical School of the University of Iowa, Iowa City, Iowa; $15,000 to the Medical School of the University of Illinois, Chicago, Ill.; $5,000 to Marquette University Medical School, Milwaukee, Wis.

The grants to Massachusetts Institute of Technology and the University of Minnesota are in addition to the gift of $1,100,000 made by Mr. Baruch in April, 1944, at which time grants were made to Columbia University College of Physicians and Surgeons, New York University College of Medicine, the Medical College of Virginia, and for minor research and fellowship programs for the advancement of physical medicine.

The present gift to Massachusetts Institute of Technology is in support of a five-year program of training and research in electronics, instrumentation, and physics in relation to medicine, to be carried on under the auspices of the Department of biology and biological engineering. It was the conviction of the Scientific Advisory Committee of the Baruch Committee on Physical Medicine that Baruch Fellows and other physicians should have more than a superficial knowledge of the physics and technology underlying the physical methods and instrumentation used in this field and it was suggested that training in this aspect might effectively be centered at the Massachusetts Institute of Technology. The program will be under the general supervision of Dr. Francis O. Schmitt, head of the department of biology and biological engineering, and under immediate supervision of Dr. K. S. Lion, assistant professor of applied biophysics, who is an expert in physical instrumentation.

The grant of $40,000 to the University of Minnesota is to support the development of a three-year teaching and fellowship program in physical medicine. The primary objective of the program is to be the furtherance of fundamental training of research workers and teachers. The program has as its basis the development of scientists in the field of physical medicine. As an auxiliary to this basic training will be developed facilities for the training of clinicians and technicians.

The other grants have been allocated from the fund of $200,000 given by Mr. Baruch in April. The sum of $30,000 was granted to Harvard University Medical School for establishment of a three-year program to provide fellowship or residencies to be used for the benefit of qualified physicians who are selected to be trained in this field. This sum will be administered by a strong standing committee on physical medicine, recently appointed by Dean C. Sidney Burwell of the Harvard Medical School, composed of Dr. J. B. Ayer, Dr. D. Denny-Brown, Dr. W. T. Green, Dr. J. H. Means, Dr. A. L. Watkins, and Dr. E. M. Landis (chairman). Appointments to the fellowships, which generally carry stipends of $2,500, will be

made annually but may be renewed to provide up to three years of specialized study and research. Emphasis will be placed upon training a few men in basic research and clinical investigation.

Unusual opportunities for clinical experience and research in the psychologic and psychiatric aspects of physical medicine will be available at Harvard. The first year will be wholly or in part devoted to basic research related to physical medicine in one of the preclinical sciences such as physiology, anatomy, or biophysics. The second year will be spent in clinical training in physical medicine at the Massachusetts General Hospital and other hospitals affiliated with the Harvard Medical School. In the third year, fellows will be assistants in physical medicine with clinical responsibilities. For candidates with extensive previous training, one-year clinical fellowships will also be granted. Applicants must have an M.D. degree from an approved medical school and a minimum of one year of internship in an approved hospital. Applications may be obtained from the Dean, Harvard Medical School, 25 Shattuck Street, Boston 15, Mass.

The sum of $30,000 is being granted to the University of Southern California to inaugurate a program of teaching and research in physical medicine in its medical school. The sum of $15,000 is granted to the University of Illinois to inaugurate a teaching program in physical medicine at its medical school. The sum of $15,000 is being granted to the Medical School of the University of Iowa to assist in a joint research and teaching program concerning the effectiveness of different methods of applying heat to the deep tissues of the human body. Finally, the sum of $5,000 is being granted to the Medical School of Marquette University, Milwaukee, Wis., for continuance of research in the physiology and pathology of nerves and muscles as related to physical medicine.

In discussing these grants Dr. Frank H. Krusen, the director of the Baruch Committee, pointed out that Mr. Baruch had been particularly interested in the important field of electronics as applied to medicine and he said that the center at Massachusetts Institute of Technology gave promise of revolutionizing the application of electronics in the diagnosis and treatment of the sick. Dr. Krusen expressed gratitude concerning the establishment of fellowships in physical medicine at Harvard and mentioned the advantage to the field of physical medicine in having this great center assume leadership in the training of fellows. He also stated that the aid given to the University of Minnesota and the University of Southern California would extend the activities of the Baruch Committee into the Midwest and Far West and thus tend to strengthen this important program. In conclusion, Dr. Krusen announced that the Administrative Board does not contemplate the recommendation of any further large grants for the establishment of additional departments of physical medicine in our medical schools. He said that the Baruch Committee would now turn its main attention toward the adequate development of the centers already established, toward providing advice in the organization of proper teaching of physical medicine in medical schools, and, through its strong Committee on War and Postwar Physical Rehabilitation and Reconditioning, would attempt to promote proper development of physical medicine in the rehabilitation and reconditioning of both military and civilian casualties of war. The Board agreed that Mr. Baruch's gifts had served as a means of providing prompt coordination of the entire program for rehabilitation of our wounded and for the provision of the trained personnel so greatly needed in activating this program.

Book Reviews

Textbook of Gynecology. By Emil Novak, M.D., F.A.C.S. Ed. 2. Baltimore, Md., 1944, Williams & Wilkins Company.

This text was published in its first edition under the title "Gynecology and Female Endocrinology." It is considerably changed in the second edition with the addition, particularly, of more complete embryologic details. A very brief chapter dealing with female urology and written by Dr. H. S. Everett has also been added.

The book has been designed for "all the needs of both students and practitioners." It is apparent that the general practitioner is meant. Many details have been purposefully omitted, particularly those of treatment and surgical technique. As such it is an introduction to the subject rather than a reference book or a complete text. It stresses to advantage the author's authoritative interest in the histologic approach to the study of gynecology.

It will interest the teacher that Dr. Novak has accepted the work of Dr. Robert Meyer dealing with the embryologic development of the vagina. It is curious that later in the book the older concept of the imperforate vagina is retained. Those who are interested will find the discussion of the anovulatory bleeding—menstruation argument entertaining.

The book has been pleasingly printed. A pair of captions have been reversed (p. 10) and one author's name is misspelled. Otherwise the book shows considerable care in detail. The reproduction of the numerous colored photographs is much the most attractive which this reviewer has seen.

Virus Diseases in Man, Animal, and Plant. By Gustav Seiffert. New York, 1944, Philosophical Library, Inc.

This book on virus diseases, purporting to be "a survey and reports covering the major research work done during the last decade," falls far short of its description. It is essentially an abbreviated description of many virus diseases, and its principal references are to literature more than ten years old. The book would appear to have some value in acquainting those not especially interested in the field of viruses with some of the basic information. It does not appear, however, that the book will be found of any significant value for those in the field.

Practical Malaria Control. By Carl E. M. Gunther, M.D., B.A., and D.T.M. (Sydney), Field Medical Officer, Bulolo Gold Dredging Limited, Territory of New Guinea, Member Australian Medical Corps, with a foreword by Professor Harvey Sutton. Pp. 91, New York, 1944, Philosophical Library, Inc.

The author of this small monograph spent several years in a highly endemic area of malignant tertian malaria in the Mandated Territory of New Guinea. In 1940, as a member of the Australian Medical Corps, he specialized in antimalarial work in Malaya. He is at present a prisoner of war.

The work is divided into four parts. Part I deals primarily with methods for controlling mosquitoes and with personal measures for protecting individuals against infections. There are many helpful suggestions offered; the pages sparkle with common sense, but, in general, the recommendations of the U. S. Armed Forces are more up to date and probably more effective. Part II is concerned with the diagnosis of malaria, including laboratory procedures and differential diagnosis.

Part III discusses treatment which may be applicable to a native population, but more recent investigations are in disagreement with the author's claim that quinine is superior to atabrin. Part IV constitutes a brief but good summary of blackwater fever.

There is no index or table of contents. More recent information than that contained in this monograph is desirable and available for students, teachers, and those interested in the problem of malaria control.

Tropical Nursing. By A. L. Gregg, M.A., M.D., B.A.O. (Dublin), D.T.M.+H. (London), L.M. (Rotunda Hospital). Ed. 2. Pp. 185, with illustrations. New York, 1944. Philosophical Library, Inc.

According to the author, this is a handbook for nurses and others going abroad. The major portion is concerned with various diseases encountered in the tropics. For each disease, the mode of infection is outlined, the methods of diagnosis are presented, and nursing care is stressed. One might well imagine the difficulties encountered when the author attempted to discuss nursing care for each of the many diseases. Some of the treatment is antiquated and amusing at times. As an example, under the treatment for sprue the author states "there is no harm in a sprue patient having a plentiful supply of literature, except that for the very anaemic reading is too great a strain. Illustrated papers may be allowed."

There is a section on laboratory procedures, and descriptive techniques for blood transfusions, intravenous injections, etc. A glossary of medical terms concludes the volume. There is an adequate index. One wonders if nurses going into the tropics this day and age will be as naïve or as poorly informed as this volume implies. Its virtue is a concise clinical description of tropical diseases.

The Dental Treatment of Maxillo-Facial Injuries, With Supplementary Material on Cases and Techniques. By W. Kelsey Fry, L.D.S., Consulting Dental Surgeon to the Royal Air Force; P. Rae Sheperd, L.D.S., Dental Surgeon, East Grinstead Maxillo-Facial Unit; and Gilbert J. Parfitt, L.D.S., Dental Surgeon, East Grinstead Maxillo-Facial Unit. Cloth. Pp. 434, with illustrations. Philadelphia, 1944. J. B. Lippincott Company. $6.50.

This American edition, in one volume, of the original edition and supplement is an outstanding addition to the literature on the subject. In condensed, readable form, it represents the results of the extensive experience of the authors at the East Grinstead Maxillo-Facial Centre and is the subject matter of lectures and demonstrations given to members of the Armed Forces. Because the sound knowledge of fundamentals is so apparent and so well expressed, it is evident that the authors have based their conclusions on ample discussion and evaluation of results in a large number of cases at East Grinstead.

All aspects of the diagnosis and treatment are discussed at length and in a most practical manner, including the numerous problems that frequently arise in the treatment of difficult fractures. This type of detailed presentation is all too frequently omitted from standard texts, the less experienced reader finding no answer to many of his problems.

The various types of fractures, including all typical fractures and resulting displacements, are discussed in detail for all regions of the mandible and maxillae. Both clinical and x-ray diagnoses are well presented with excellent subject matter on the interpretation of roentgenograms, and the technique of the various x-ray projections is well illustrated. The chapter on general health and feeding is full of worthwhile, helpful information, very valuable to the novice. The fundamental considera-

tions of bone repair are discussed at length, including normal bone repair and various complications such as the source and spread of infection, necrosis, and nonunion.

The principles of fracture treatment and surgical techniques are described and well illustrated. The authors favor cap splints for most cases. These have been somewhat modified since the World War I experiences of the senior author. The pin tube (hinge) type of locking devices almost universally used at that time are not shown in this text.

Complete instructions are included for the construction of splints and locking devices as well as for the construction of oral prostheses to replace missing portions of the jaws. Several of the wiring and arch bar methods so commonly used in America are well illustrated.

Colored photomicrographs depict the histologic structure of normal bone, reaction to injury, bone absorption, repair, and fibrous union.

Numerous case histories of patients with fractures are profusely illustrated and described in detail, with progress notes, providing excellent subject matter for study.

The authors' conservative point of view on skeletal fixation is to be commended as they stress the fact that the appliances are not very strong and that additional indirect fixation of the teeth in occlusion is desirable in most cases.

This book, by far the best text on the subject, meets a real need. Although the authors state that the book is primarily intended for dental surgeons with little or no experience in this subject, the most experienced oral surgeons will find it worth while reading from cover to cover. The text is so well arranged and so extensively illustrated that it may be highly recommended.

Metabolism Manual. By Jessie Lex, R.T., M.T. (ASCP). Pp. 56. Baltimore, Md., 1943, The Waverly Press.

This book highlights the many technical and psychologic factors involved in obtaining good determinations of basal metabolic rates. This type of information has heretofore not been readily available in print.

The manual will make useful reading for the technologist who has experienced difficulty with metabolic determinations. The wisdom of the meticulous instructions to patients which the author recommends will be questioned by many.

Textbook of General Surgery. By Warren H. Cole, M.D., F.A.C.S., Professor and Head of the Department of Surgery, University of Illinois College of Medicine, Chicago, and Robert Elman, M.D., Associate Professor of Clinical Surgery, Washington University School of Medicine, St. Louis, Ed. 4. Pp. 1118, with 559 illustrations. New York and London, 1944. D. Appleton-Century Company, Inc. $10.

A new edition now is real determination. This edition does not entail the extensive revision of the last one in 1941. Material has been rearranged with additional pages to bring the text up to date on subjects of current interest such as chemotherapy and hypoproteinemia. A chapter of considerable length on War and Catastrophe Surgery has been added. It includes a discussion of newer types of war injuries such as the crush syndrome, immersion foot, and blast. Practical points are made regarding front-line first aid and anesthesia, and the problems of transportation and priority of treatment.

The style is clear and direct throughout. Subjects are handled concisely and the reader is, correctly, referred to the literature for details. The bibliography is well chosen for the student reader. Its extent is satisfying but not terrifying. Organization and illustrations are good. Physiologic and pathologic relations are given briefly

but adequately. Therapeutic measures are stated and the rationale outlined, but operative details are avoided.

As in the third edition, the authors have made an attempt to combine the advantages of single and multiple authorship by writing the text themselves and then having the material reviewed by specialists in each field. The advantage of single authorship by men gifted in writing as well as in medicine has been much underrated in recent years. A lucid and readable portrayal is an advantage anywhere but is obligatory in a student text. The authors' attempt to preserve these characteristics while avoiding the criticism of a lack of breadth of view is to be commended and encouraged.

A common fallacy of publishers is the belief that the same type of textbook material can be successfully presented to general practitioner, casual surgeon, and third-year medical student. A moment's reflection on the diversity of experience and point of view in these groups reveals the absurdity of this thesis. The authors of this book are to be congratulated in selecting one reader, the medical student, and successfully presenting surgical material to him. The book contains, however, a surprising amount of valuable material for the more experienced reader.

Técnica Cirúrgica Abdome. In two volumes. By Alfredo Monteiro, Professor of Surgery at the University of Brazil. pp. 1205, with 1248 illustrations. Rua Sete de Setembro, 180—Rio, 1943. Editora Scientifica.

The author has a good summary of the general principles of surgery, as well as anatomy, physiology, and pathology of the different organs in which the operation is to be performed. The physiologic and pathologic aspects of the ulcer problem are well discussed and are up-to-date. A number of techniques are described to resect and anastomose the bowel, both by the open and aseptic methods, affording the surgeon a wide field of choice according to his personal skill and the circumstances of the case.

The chapter on hernias is well done and nicely illustrated with clear diagrams.

An extensive part of the first volume is devoted to surgery of the stomach, including most of the techniques of North American, as well as those of South American, surgeons. The surgery of the gall bladder and common duct is well described and the author points out the most common mistakes made in this type of surgery.

The chapter concerning the problem of bowel obstructions has a good discussion, and shows the way this syndrome is treated by several surgeons, Gatch, Cokkins, and others. The author considers the ideas of Wangensteen on this subject the most physiologic, and he follows them.

A good portion of the second volume is concerned with the surgical treatment of carcinoma of the rectum and the results achieved.

To this reviewer, from one of the spanish-speaking countries, it appears a firm step toward forward progress in surgery, for all the Spanish-speaking countries.

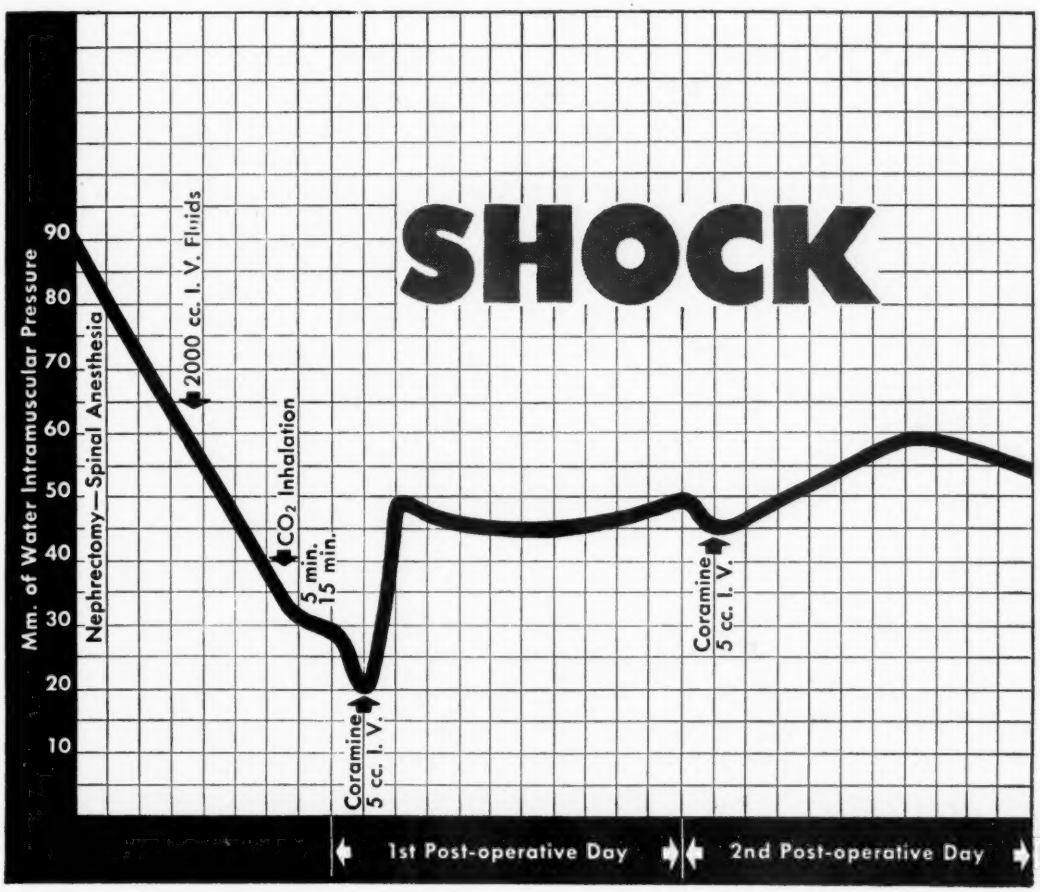
Treatment of Peptic Ulcer. By George J. Heuer, M.D., Professor of Surgery of Cornell University Medical College and Surgeon-in-Chief of the New York Hospital, with Cranston Holman, M.D., Assistant Professor of Clinical Surgery, Cornell University Medical College, and William A. Cooper, M.D., Assistant Professor of Clinical Surgery, Cornell University Medical College, Philadelphia, Pa. Pp. 118. Philadelphia, 1944. J. B. Lippincott Company. $3.

The authors review a ten years' experience with the treatment of ulcer at the New York Hospital. They present a well-studied account of patients after medical management, gastrojejunostomy, and gastric resection. Their results appear to sug-

gest that the remote results in duodenal ulcer after gastrojejunostomy are within 10 per cent of being as good as those following gastric resection. Their reported incidence of gastrojejunal ulcer after gastrojejunostomy is 25.9 per cent.

Inasmuch as the authors express a preference for the small gastric resection over more extensive resections, it is not surprising that they are disappointed over the failure of gastric resections to protect against recurrent ulcer. They stress the importance of removing the pylorus and antrum but fail to indicate the length of the afferent duodenojejunal loop, an item of some considerable importance apparently in determining whether recurrent ulcer will follow gastric resection. Though many will not agree with the authors in their reawakening of interest in gastrojejunostomy as a suitable operation for duodenal ulcer, everyone who has an interest in the ulcer problem will find study of the tabular data profitable and interesting.

The authors favor gastric resection over gastrojejunostomy for the following conditions: (1) Gastric or duodenal ulcer complicated by hemorrhage, (2) gastric ulcer, and (3) recurrent ulcer. They are not in complete accord with recent expressions from surgeons suggesting that resection should be undertaken more frequently for gastric ulcer, if only in the interests of resolving the confusion which may exist between ulcer and cancer. On this score, the authors appear to have had more success than others in differentiating ulcer from cancer. They find the presence of a good response to the histamine test a better differential than the x-rays. As a matter of fact, they believe that gastric analysis constitutes an agency almost infallible in diagnostic accuracy in distinguishing between gastric ulcer and cancer (page 26). Very few, if any, who have studied this question critically will be able to subscribe to this thesis of the authors.



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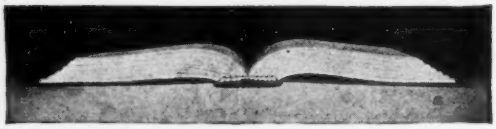

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